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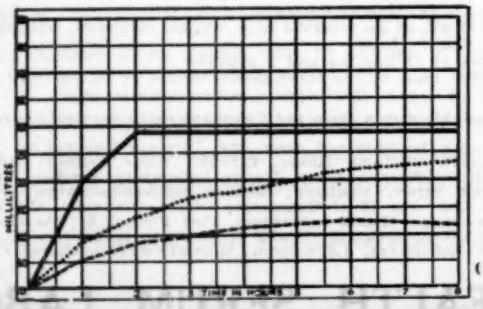
Hydrochloric acid neutralised by 1 gramme Magnesium Trisilicate (dried at 100° C.)



This graph is described in the paragraph on Magnesium Trisilicate.

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SUPPLEMENT NUMBER 24 ON WAR MEDICINE AND SURGERY:
The Present Position of the Vitamins.

WITH THE AUSTRALIAN ARMY MEDICAL CORPS IN TWO SIEGES: ANZAC AND TOBRUK.[1]

By C. MORLET, D.S.O.,
Major, Australian Army Medical Corps, Australian Imperial Force.

THE following narrative is intended to present briefly a picture of those two famous campaigns, Anzac and Tobruk, as they appeared to the eyes of a medical officer who saw service in both: it is in no sense a historical record, and if there are inaccuracies in details it is to be remembered that this account is based solely on personal experiences and impressions.

The actual circumstances of the sieges of Anzac and Tobruk were remarkably alike; in each case an Australian force was beleaguered on a narrow strip of Mediterranean coast; the only source of supply was sea communication, by a hazardous voyage exposed to attack and subject to the vagaries of weather along a rugged shore. Disembarkation of reinforcements and stores was, in each case, subject to hostile interference, and in the main was confined to hours of darkness.

In each case the campaign lasted for seven months—the same months, from April to November. Climate was practically the same during the summer season, and included the hottest months with the attendant problems of flies, vermin and water shortage. The twenty-six years of progress intervening between the two campaigns produced remarkable changes in weapons and warfare; yet in living conditions, among the striking contrasts, were to be found many points of resemblance. For instance, a little beach in Tobruk harbour, where many of us used to swim on the hot evenings, was always known as "Anzac Cove" and was exposed to the occasional attentions of "Bardia Bill", as its ancestor was harassed in the old days by "Beachy Bill".

[1] Read at a meeting of the Western Australian Branch of the British Medical Association on April 21, 1943.

Anzac.

In speaking of Anzac, I realize that many of you, from personal experience, will be more familiar with the conditions there than I am. To you fellow Anzacs, my description will be merely a dreary portrait of the old scenes which for twenty-seven years you have been trying to forget.

In the landing at Anzac on April 25 I did not participate, being at that time in Egypt serving with the First Australian General Hospital, with which unit I had left Australia. It was not until midsummer, when the campaign had become stabilized, that I received a movement order to Anzac, and joined the 10th Battalion as regimental medical officer, replacing captain Harry Nott, who was evacuated suffering from typhoid fever.

Compared with the thrill of the Anzac landing and attack, my own arrival as a replacement was very uneventful, and in exactly the same manner, twenty-six years later, did I come to Tobruk.

Leaving the base area, which in 1915 was at Cairo and in 1941 at Gaza, in each case I set forth from the First Australian General Hospital and with a few companions travelled slowly along lines of communication, encountering many delays at the different stages. In each case the last section of the journey was made at night in a destroyer and ended by my hauling my kit ashore in the darkness, to finish an uncomfortable night at the waterside. In this way, after the short trip in a destroyer from Mudros, where I had been delayed for some days, I finally found myself at Anzac at a time when, in the midsummer heat, the uncomfortable living conditions and widespread sickness were more a feature of the siege than was the actual fighting.

At this stage the military situation appeared to be, briefly, as follows. The final attack on the ridge at Sari Bair, with the landing at Suvla Bay, had just petered out. Both the First Australian Division and the Anzac Division had suffered terrible casualties, and Lone Pine with other costly attacks on Turkish trenches had simmered down. Stalemate seemed to have been accepted by both sides,

and siege conditions had become well established. Summer was at its height and the disease figures were mounting rapidly. "Line of communication" was recovering from the rush of casualties resulting from this costly operation, and evacuation was at last proceeding smoothly from Anzac—with the comforting spectacle of a hospital ship almost always at anchor in the Roads, and prepared to take serious cases at any time.

The regimental aid post of the Tenth Battalion was dug into the side of Artillery Road, at the entrance to Lady Galway Tunnel, on the right of Lone Pine. Field guns of the Eighth Battery were close around, and drew on us the regular daily bombardment which was known as the "morning and evening hate", a very noisy affair, which frequently caught us at meal times. All supplies came up from the beach, and there being no motor transport whatever, everything was man-handled to the forward units, or where possible, carried by pack mule. This weary routine of ration and water fatigues, and the incessant man-handling of ammunition, must have done much harm to both morale and physique during those summer months.

Turkish reconnaissance aircraft occasionally sailed over us at (we then thought) a great height, and we used to watch with interest the unfolding puffs of shrapnel in the air, as these ancestors of "ack ack" made great efforts to reach the primitive planes. I heard rumours of darts and iron spikes being dropped by Turkish planes; but I never heard of an aerial bomb being dropped at Anzac.

The days were intensely hot, and throughout August and September the black clouds of flies were simply beyond description and literally followed one's food into one's mouth. Housing was entirely in dugouts, either cut into banks and trench walls, or merely in holes partly covered by ground sheets.

All ranks "stood to" each morning, just before dawn, until daylight, in the forward units. Diet was monotonous, and food was almost entirely tinned. The issue of fresh meat to the battalions was discontinued during the hot months even if it was landed, as it invariably reached the forward units in a fly-blown condition. Fresh vegetables, except for onions and sometimes potatoes, were unknown. The staple food was bully beef, biscuit and jam, occasional issues of rice, and bread from the bakeries at Imbros. Water was strictly rationed; it came partly from wells and was partly landed from ships. It was man-handled in two-gallon tins by the water fatigues, and where practicable distributed by pack mules. I forget the actual ration, but I kept a half-kerosene tin hidden in my dugout and put a little water in it each day, so as to have a fresh-water bath on Sundays.

Swimming at the beach was the great luxury, but entailed the long scramble down and the weary toil up the heights again in the heat, apart from the risk of interruption by "Beachy Bill", which took such terrible toll of bathers on Anzac Beach.

Sick parade was a dreary procession of jaundiced, diarrhœa-stricken lads. As a general rule, "sticking it out" was a point of honour with all ranks, and evacuation on account of sickness often involved a heated argument with the patient. Diarrhœa was universal, and most of the troops were infested with lice. Battle casualties, however, at this time were not heavy, though there was a steady trickle of them. The troops were hardened campaigners by now, and kept well under cover. Water fatigues and ration parties were "strafed" on tracks and roads at night, when most of the casualties occurred. The Thomas splint was not available, and the splinting of fractured thighs was difficult in consequence. The injection of antitetanic serum had just been made a routine procedure in all wounds. The principal diseases were intestinal—dysentery, typhoid fever and diarrhœa. Jaundice, septic sores and barcoo rot were common, while dental caries and broken teeth were a troublesome problem to the regimental medical officer in the absence of any dental officers or dental units.

Evacuation from the regimental aid post was by a good long "carry" to the advanced dressing station. Casualties among the bearers at this time were infrequent, though the "carry" was arduous and in some places exposed. Ambulance cars were never seen at Anzac, and evacuation from the advanced dressing station was by relays of bearers to the beach, where the First Casualty Clearing Station and later the First Stationary Hospital organized the evacuation of such men as were not held and treated in riveted tents and dugouts.

From the beach, which was intermittently shelled, serious casualties were ferried out to the hospital ship by tugs or barges, and here normally all major surgery was done. In times of emergency, as occasionally occurred in rough weather, such men could be held for a time, and much good work was done at the hospital on the beach. Less urgent casualties were embarked at night on mine-sweepers, which took them to Lemnos, returning with reinforcements and stores.

Shortly after I arrived at Anzac hygiene was placed under the supervision of divisional hygiene officers. Previously it had been the responsibility of the assistant provost marshal and provost corps. The new divisional hygiene officers did their best to cope with an impossible problem. Fly-proof latrines I never saw; I heard later, when at Lemnos, that fly-proofing material began to reach Anzac just before the evacuation, when the flies had gone! Deep open trenches, with a rail, crowded all day with sick-looking troops, dense clouds of flies and an occasional shrapnel burst to help things along—this was the familiar routine of Anzac sanitary arrangements.

The summer faded, and the flies began to die out in October. Towards the end of November the Tenth Battalion was taken off on a cold night amid heavy rain, but without a casualty. The weary remnant reached camp at Lemnos, where they were further thinned out by paratyphoid fever and cerebro-spinal meningitis before finally getting back to Egypt.

Such, briefly, was Anzac as I saw it from August till the end of November.

Tobruk.

Twenty-six years later I was again summoned from my work in the eye clinic of the First Australian General Hospital to replace a casualty in a forward unit, namely, the Fourth Australian General Hospital at Tobruk. Again I experienced the series of delays and difficulties attendant upon a journey on lines of communication as an unattached detail. Again the final stage was in a destroyer, and I ultimately reached Tobruk in pitch darkness on Friday, June 13. In spite of the date, the journey on that occasion was without incident; though the same destroyer was sunk a few days later on the same voyage.

No time was lost in bundling the reinforcements ashore and unloading stores and ammunition. In little more than half an hour, the destroyers (of which there were usually two) had vanished from the harbour, and were dashing for Egypt again, through hostile waters infested with shore-based aircraft.

This regular nightly visit of the Navy was for months our sole means of intercourse with the outside world, with the exception of occasional fleeting visits from small supply ships, which made the passage at great risk and suffered very heavy casualties. We depended on the destroyers for reinforcements and ammunition, for stores and for mail, and they took away our casualties on their return journey. The voyage took from ten to twelve hours, and was often full of excitement and sometimes terribly costly.

On the night of my arrival, we got ashore just in time for an air raid on the harbour, in which the town and hospital participated, and I spent the rest of the night at the water-side in a capacious cave fitted out as a hospital. This place, known as the "docks hospital", was the descendant and counterpart of the casualty clearing station on Anzac Beach. An elaborate, concrete-lined cavern, tunnelled into a cliff at the waterside, the docks hospital was electrically lit and had accommodation for 70 or 80 stretcher cases, and many walking wounded. Evacuation of all casualties from Tobruk took place from here at night, by means of the visiting destroyers. During moonlit periods there was no evacuation, as the sea voyage was

then far too hazardous, and at these times casualties were held, both at the docks hospital and at the Fourth Australian General Hospital, which sometimes held upwards of 1,000 patients. At these times, too, we were without mail, and could get no fresh supplies.

Tobruk harbour, I found, was quite a contrast to the scrubby heights of Anzac. A narrow tongue of blue water, cutting into the barren coast, the harbour was locked within shores of bare, yellowish earth, strewn with stones, and sloping up to rounded hills, devoid of vegetation. The town—completely in ruins—was, when viewed from a distance, grimly picturesque; all the buildings were of gleaming white concrete and stone, contrasting with the tawny desert around, and reflected in the blue water, on the edge of which Tobruk arose. In the centre of the town, among the white ruins, stood the church, of which the tower remained untouched to the last.

Though the waterfront went by the proud title of "The Docks", there were no dock installations in use. The harbour was fringed with wrecks and hulks, ships of all sizes that had been sunk and were aground in the shallows near the shore; to these, newcomers would tie up in the darkness and nestle close, in order to escape the watchful eyes of enemy reconnaissance planes which constantly hovered overhead. Unloading was done mainly by lighters, and for the most part at night. As the nearest enemy aerodrome was only 32 miles away, flocks of Stukas would be overhead in a few minutes on sighting a newcomer or any undue activity in the harbour, and daylight work was very risky and costly.

The Fourth Australian General Hospital was partly housed in Italian barracks, on the slope of a barren hill overlooking the town, and about 400 yards from the water. The medical wards were detached and were in brigaded tents, well dug into the stony ground near the open sea about two miles from the barracks; they were known as the "beach hospital". Here the staff of the medical division lived with their patients, in dugouts and sunken tents. The surgical wards and staff, with special departments and administration, were much more comfortable in the roomy, stone-walled barracks, where a party of Italian prisoners were employed as stretcher bearers and were kept busy most of the time.

Living conditions for those of us residing at the barracks were a vast improvement on those of Gallipoli. In fact, apart from a monotonous diet of tinned food and the water restrictions, we had little to complain of.

The lot of the troops on the perimeter, however, was little if at all more comfortable than in the old Anzac days. Admittedly, at Tobruk, the dugouts, tunnels and caves were on the whole far more elaborate than at Anzac. The terrain, however, made living conditions intensely uncomfortable—arid, stony desert in all directions, with clouds of dust constantly drifting to and fro, and the complete lack of shelter from the grizzling sun and glare rendered water restrictions a real hardship. The water ration was six pints per man per day for all purposes; hospital patients and staff were able to supplement this, but for the fighting troops it was scarcely enough for bare necessities, and left nothing for washing clothes or person. Moreover, the issue water was brackish and heavily chlorinated, and it made tea taste all wrong. The hospital, however, was able to obtain a supply of fresh water by sea from Egypt. Sea bathing when possible was the great luxury. Tinned foods were of better quality and greater variety than in the old Anzac days, and cooking facilities were usually much better.

The Work of the Australian Army Medical Corps.

The work of the Australian Army Medical Corps presented a most striking contrast in a variety of ways with its work in the earlier siege. This was due mainly to the march of progress in the twenty-six years which separate the two campaigns, and also in some degree to facilities dependent on local conditions. There seemed to be three outstanding factors which were mainly responsible for the altered picture of Australian Army Medical Corps work—namely, hygiene, transport and aerial attack.

Hygiene.

In hygiene, local facilities allowed of immense improvement. The squalid conditions imposed by the cramped campaign of 1915 were replaced by first-rate sanitary arrangements. In Tobruk, throughout the summer, two efficient hygiene sections operated, one being responsible for the forward units and perimeter and the other for Tobruk area. Undoubtedly the work of these units did much to prevent any disease crisis comparable with that at Anzac.

Flies there were in swarms; but the protection afforded by sanitary precautions kept the position under control throughout the hot weather.

Lice were not nearly so prevalent as they had been at Anzac, but the whole area was infested with fleas. A not uncommon source of severe burns was the practice of drenching dugouts with petrol and then throwing in a lighted match, with the object of exterminating fleas.

Dust, which was never a great feature at Gallipoli, was simply beyond description at Tobruk—a fine reddish powder, which gritted in the teeth, permeated the food and lay thickly in the hair and eyebrows; it crept into every crevice, and often thickened the atmosphere to a dense fog. A goldfields man told me that after living for years at Coolgardie, he thought he knew all about dust storms—until he got to Tobruk!

Transport.

Transport facilities were responsible for another striking contrast in Australian Army Medical Corps work as between the two sieges. Gone were the old heart-breaking ration and water fatigues—the strings of men with two-gallon water tins, the loaded pack mules and weary stretcher parties struggling through the tracks and gullies of Anzac. In 1941, motor transport completely changed the picture. Ration and water convoys rumbled to and fro all night, and troop movements by means of trucks and carriers, motorized artillery, tanks and armoured cars formed a truly remarkable contrast.

Broad bitumen motor roads linked the hospital on the one hand with the docks and harbour, and on the other with the positions on the perimeter, both east and west. Along these arteries streamed ambulance cars, often travelling direct from regimental aid post to hospital, and saving innumerable lives by rapid and efficient evacuation. Between the main roads, the network of tracks in the stony ground were usually very rough going, but for the most part negotiable for wheeled traffic.

Aerial Attack.

Aerial attack constituted the most dramatic contrast in the fighting of the two campaigns, and profoundly influenced the work of the Australian Army Medical Corps. The "ack ack" barrage over Tobruk harbour was considerable, especially in the later months, but of aerial defence there was none. The nearest allied aerodromes in use were far away to the east, and could afford no fighter protection whatever. Occasionally, one or two friendly planes would pay a brief visit to the area, circle round for a few minutes and then make off eastwards again. Their departure would often be the signal for a raid, and enemy planes would be overhead as soon as they were out of sight.

The perimeter was ringed about by enemy aerodromes, and the familiar drone of reconnaissance planes overhead was often the prelude to dive-bombing attacks on the harbour and town—the so-called "Stuka parades". Apart from these displays, high-level bombing was almost incessant, being carried out usually several times a day. Moonlight nights produced a constant procession of aerial visitors, and the dark nights were periodically illuminated by flares and incendiary bombs. The hospital buildings at the barracks, situated close to the harbour and surrounded by legitimate targets, participated in much of this aerial attack, and came in for a tremendous amount of bombing, which was probably never deliberate. The buildings themselves formed excellent protection from splinters, as the walls were sturdily built of stone and

concrete. The roofs, however, of tiles, were designed only to keep out the sunshine, and afforded no protection from a direct hit.

At the end of the siege, nearly all the wards had holes in the ceilings, and some were badly smashed by direct hits. Everywhere the heavy walls were gashed and scarred, though never, I think, actually penetrated by splinters.

Efficient shelters were established at the entrance to each ward, and to these such patients as could walk repaired during raids, while those who were confined to bed lay helpless, listening to the din and hoping for the best. The medical wards on the ocean beach, owing to the proximity of coastal and "ack ack" batteries, had a big share in all this—in fact, at one stage they had actually the worst of it, in their dugouts and sunken tents.

Evacuation from the hospital took place after sunset on dark nights by ambulance cars, and the casualties were transferred to the docks hospital at the waterside. Here, for tense and interminable hours, they lay and sat, crowded together, anxiously awaiting the coming of the destroyer to convey them to Egypt and comparative safety. Though on each voyage these ships ran the gauntlet through hostile waters, it was exceptional for the actual process of embarking casualties to be interrupted. The operation was rushed through in the minimum time possible, and the ships were gone again with surprising smartness. Often the harbour would be illuminated by flares and bombarded both before and after embarkation.

Types of Casualties.

Battle casualties at Anzac were for the most part caused by shrapnel, high explosive or bullet wounds; but at Tobruk a high percentage of wounds were due to bombs. The terrible rending injuries produced by grenades, land mines and booby traps were not uncommon; these weapons in modern warfare have attained a diabolical perfection. Such injuries not infrequently involved the loss of one or both hands, and the impaction of incredibly numerous and minute foreign bodies of copper, aluminium or some alloy, which were very destructive, especially to the eyes.

Desert sores and skin infections were as common and intractable as the old barcoo rot and festering sores of Anzac.

In disease, Tobruk had its share of dysentery and diarrhœa; but the wholesale incidence which was a feature of Anzac was never encountered. New conditions, such as relapsing fever, kept the pathologist busy, and reinforcements ensured that the venereal diseases wing was never idle. The establishment of dental units was a notable advance on the old Gallipoli days, and an enormous amount of dental work was done.

Disposal of Casualties.

Whereas at Anzac practically all major surgery and treatment of serious medical casualties was undertaken on the hospital ship, to which evacuation was in the quiet times comparatively easy, at Tobruk this work was undertaken by the Fourth Australian General Hospital. This unit, a 600-bed hospital, fully equipped with X-ray facilities, pathological laboratory and special departments, remained at work throughout the siege. Here all branches of surgery were undertaken, a blood bank for transfusion was maintained and hundreds of medical patients were treated until returned to duty.

During the moonless nights of October, the Australian force was relieved, unit by unit. As at Anzac, the siege terminated for the Australian Imperial Force with evacuation by sea, and was almost as triumphant a success.

Conclusion.

To have served in two campaigns with so many features in common, yet with such striking contrasts, has been of unique interest.

But to me, by far the most interesting feature of each is the fact that now it is only a memory.

THE PATHOGENICITY OF WASHED CLOSTRIDIUM WELCHII AND THE MODE OF DEVELOPMENT OF CLOSTRIDIUM WELCHII INFECTIONS IN MAN.

By HILDRED M. BUTLER,[1]

From the Department of Pathology, Women's Hospital, Melbourne.

IT is still stated in text-books, and it appears to be accepted by most bacteriologists, that cultures of *Clostridium welchii* freed from toxin by washing or by growth on a solid medium are not pathogenic for the guinea-pig.

During the course of experiments carried out in this laboratory to distinguish strains of *Clostridium welchii* causing fatal abortional infections from strains which cause mild infections, a number of cultures of *Clostridium welchii* freed from toxin were tested in guinea-pigs. These experiments showed that all the strains from fatal cases and many from mild infections produced a fatal gas gangrene in guinea-pigs when washed bacilli were injected intramuscularly. Later work revealed that some strains from cases of post-traumatic gas gangrene and some isolated directly from cultivated soil were also pathogenic for guinea-pigs when washed bacilli were used.

The Pathogenicity of Washed Clostridium Welchii when Freshly Isolated.

The experiments were carried out as follows. The strains were grown on agar slopes in a McIntosh and Fildes jar for twenty-two hours. The growth from two slopes was emulsified in saline solution (0·85% sodium chloride) and centrifuged, and the deposit of organisms was resuspended in saline solution at a density of approximately 2,000 million per cubic centimetre. In this way the organisms were not only grown on a solid medium, but they were also washed once with saline solution. The saline washings failed to produce the opalescence in human serum and egg yolk which is characteristic of the presence of *Clostridium welchii* toxin, so it appeared certain that the bacterial suspensions injected into the guinea-pigs were free from toxin. Various quantities of the suspension were injected intramuscularly into guinea-pigs weighing from 250 to 300 grammes. Two guinea-pigs were used for each test.

Seventy-three strains have now been studied in this fashion. Each strain was tested within three months of isolation and in some cases within a few days. Thirty-nine strains produced fatal gas gangrene when the infecting dose was 0·2 cubic centimetre of suspension, and ten others produced a fatal infection with a dose of 0·5 cubic centimetre. Thus two-thirds of the strains tested were pathogenic when organisms freed from toxin were used. Further experiments showed that the injection of 0·1 cubic centimetre of suspension intramuscularly sometimes produced fatal gas gangrene, and that in some instances subcutaneous inoculation also gave rise to fatal infections. Washing of the bacilli two or three times instead of once did not alter the results obtained.

The Effect of Artificial Cultivation.

Twenty-five of the strains which proved pathogenic for guinea-pigs when washed bacilli were injected were retested after various periods of artificial cultivation in meat broth. The cultures were kept at a temperature of 5° C. and were subcultured every three months. In the retesting of these strains the inoculation dose was 0·5 cubic centimetre of suspension. The results obtained are shown diagrammatically in Figure I. The first column indicates that washed bacilli from each of the strains when first tested were pathogenic for guinea-pigs. The unshaded portions of the other columns indicate the number of strains that had lost the power of killing when washed bacilli were used after various periods of artificial cultivation. After nine months nearly half the strains, and after eighteen months all but three of the strains, had lost the power to kill when washed bacilli were used.

The Relationship between Pathogenicity of Washed Bacilli and Certain other Characteristics of Clostridium Welchii.

Past work in this laboratory has shown that, in *Clostridium welchii* infections following abortion, the severity of infection

[1] Work done with a grant from the National Health and Medical Research Council.

depends primarily on the nature of the infecting strain, the pathogenicity of which is closely correlated with growth characteristics, capsulation and resistance to phagocytosis (Butler[1] [3] [5]). To judge by the experiments with washed bacilli so far carried out, the ability of such suspensions to kill guinea-pigs is more common than those characteristics which we in this hospital regard as determining exceptionally high pathogenicity for human beings. Severe infections following abortion are caused by heavily capsulated strains only, and in the majority of such cases the infecting strain, in addition to producing a large amount of α toxin, is a smooth variant and resistant to phagocytosis by human leucocytes. There is no close correlation between any of these characteristics and the ability of washed bacilli to kill guinea-pigs.

For example, although strains which were pathogenic when washed free from toxin were very common amongst the heavily capsulated variants, such strains were also found in the less capsulated groups. Thus, in this series, 29 out of 38 heavily capsulated strains were pathogenic when washed bacilli were used. But so also were 10 out of 18 moderately capsulated strains and nine out of 17 poorly capsulated strains. This lack of correlation between the pathogenicity of washed cultures and the amount of capsular material produced in broth was also apparent when the strains were retested after various periods of artificial cultivation. Some of the strains which had lost their power to kill as washed bacilli showed no change in capsulation, while there were others which, although producing much less capsular material than when first isolated, were still pathogenic for the guinea-pig under the conditions of these experiments.

A similar lack of correlation was observed between the pathogenicity of washed bacilli on the one hand and both colony form and resistance to phagocytosis by human or guinea-pig leucocytes on the other.

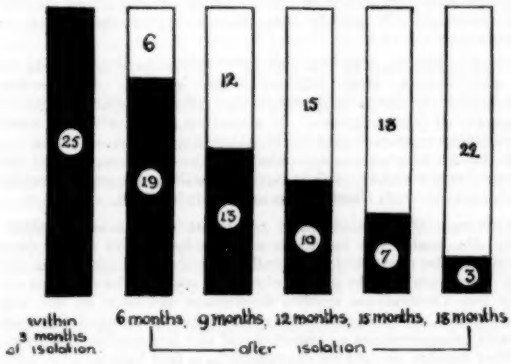

FIGURE I.
Loss of pathogenicity during artificial cultivation.

The Mode of Development of Clostridium Welchii Infections in Man.

The findings here reported, that washed bacilli from so many strains of *Clostridium welchii* were pathogenic for the guinea-pig, are in striking contrast to most of the results obtained during and shortly after World War I. Bullock and Cramer[4] found that of more than 100 test animals inoculated with 0·5 cubic centimetre of a dense suspension of washed *Clostridium welchii*, only one developed fatal gas gangrene. The Medical Research Council Committee upon Anaerobic Infections, in 1919,[5] reported a similar experience in regard to the lack of pathogenicity of washed organisms, and modern text-books still accept this view, although in De Kruif and Bollman's[6] paper in 1917 it was clearly shown that washed bacilli from some strains were pathogenic for the guinea-pig. But this last finding was apparently overshadowed by the tremendous increase in pathogenicity observed by these workers when the toxic culture filtrate was injected together with the washed bacilli.

The contention, which I believe to be erroneous, that *Clostridium welchii* strains in general when free from toxin are unable to initiate infection, appears to have arisen because most of the strains isolated during World War I were probably not studied until some considerable time after their isolation. The results given in this paper show how unlikely it would be that after a lengthy period of artificial cultivation many strains could still cause infection when free from toxin.

The assumption that the introduction of *Clostridium welchii* into human wounds causes serious infection only in the presence of large amounts of damaged tissue, of foreign bodies, of interference with the blood supply *et cetera*, was largely based on this supposed lack of pathogenicity of washed bacilli. Since the *Clostridium welchii* organisms introduced into a wound are free from toxin, it was held that tissue damage *et cetera* were essential to enable these organisms to gain a foothold, and that the toxin produced as the result of growth in the damaged area paved the way for a spreading infection by damaging the adjacent tissues. The demonstration, therefore, that the bacilli themselves are frequently able to cause a fatal infection in the guinea-pig in the absence of extensive tissue damage, makes necessary a critical examination of the mode of development of *Clostridium welchii* infection in man.

The report of the Medical Research Council Committee upon Anaerobic Infections[5] has already shown the inadequacy of the attempt to explain the development of gas gangrene on the basis of the lack of virulence of the bacilli themselves. After discussion of the part played by damaged tissue, interference with the blood supply, the presence of foreign bodies, certain salts, cold, fatigue *et cetera*, in enabling the supposedly avirulent bacilli to cause gas gangrene in man, these workers were forced to conclude that, "after giving due weight to all these facts and possibilities it cannot be said that they are sufficient to explain the occurrence of gas gangrene in the majority of cases".

In *Clostridium welchii* infections a satisfactory explanation of the mode of development is afforded if we regard the strains of this organism as divisible into groups according to their invasiveness—that is, the power of the bacilli themselves to invade the tissues. A study of some hundreds of freshly isolated strains of *Clostridium welchii*, and consideration of the lesions produced in the patients as the result of the presence of these organisms, lead me to suggest the following three groups.

The first and most important group consists of those strains which are so highly virulent that they can invade healthy tissue and cause a severe infection in the absence of large amounts of damaged tissue, of interference with the blood supply, of foreign bodies *et cetera*. Such strains are usually smooth variants, are extremely heavily capsulated, are resistant to phagocytosis even in the presence of *Clostridium welchii* antitoxin and are pathogenic for the guinea-pig in the absence of preformed toxin. These highly invasive variants are comparatively rare.

Secondly, there are strains of moderate invasive power, which do not readily invade healthy tissue, but which can spread rapidly in damaged areas, thus producing sufficient toxin to damage adjacent tissue and thereby occasion a spreading infection. In the absence of extensive tissue damage, strains such as these are unlikely to cause severe infections in man. These strains show some, but not all, of the characteristics of highly invasive variants. As a rule they do not produce typically smooth colonies, and they are less heavily capsulated and less resistant to phagocytosis than the highly invasive strains. Some are pathogenic for guinea-pigs when washed bacilli are used.

Thirdly, there are strains of low invasive power, which probably multiply only in dead tissue and cannot invade adjacent areas even if these are damaged by toxin, so that a spreading infection, which is the essence of gas gangrene, is never produced by such strains. As a rule these strains produce rough colonies, are poorly capsulated, are readily phagocytosed, and fail to kill guinea-pigs when washed bacilli are used. Occasionally a strain of low invasiveness possesses one or other, but never several, of the characteristics of the more virulent organisms.

The fact that strains which are only moderately invasive for man are sometimes pathogenic for guinea-pigs in the absence of extensive tissue damage and preformed toxin, suggests that human tissues may be more resistant to *Clostridium welchii* infection than those of the guinea-pig. Colony form, capsulation and resistance to phagocytosis appear to be more reliable than the pathogenicity of washed bacilli for guinea-pigs as an indication of invasiveness for man.

Work carried out at this hospital has shown that only the highly invasive strains cause severe abortional infections. In such cases there is no correlation between the severity of infection and the amount of local tissue damage. A limited experience of post-traumatic gas gangrene has shown that fulminating infections may be caused by variants with exactly similar characteristics to those causing the severe abortional infections, while the strains responsible for gas gangrene of moderate

severity developing in an extensively damaged area never possess all the characteristics of highly invasive variants. It is my opinion that not only the severe abortional infections, but all cases of severe *Clostridium welchii* infection developing in the absence of extensive tissue damage, are caused by highly invasive strains and by these strains only. According to this view, gas gangrene following the hypodermic injection of a bland substance or any other trivial injury is due to the introduction into the tissues of a strain so highly invasive that it can cause a rapidly spreading infection in the absence of extensive tissue damage.

The existence of strains of *Clostridium welchii* which are sufficiently invasive to cause infection in man in the absence of extensive tissue damage or of lowered general resistance, offers one explanation for the statement of the Medical Research Council Committee already quoted. It is probable that the cases studied by these workers included a number of infections with highly invasive *Clostridium welchii* strains.

The failure in the past to recognize the occurrence of strains of extremely low invasive power—strains which cannot invade even damaged tissue—has led to difficulties in the interpretation of clinical and experimental findings.

Robertson and Keppie[7] showed that toxin production alone did not determine the ability of *Clostridium welchii* when present in a wound to cause a recognizable infection. They found that strains which did not cause a typical infection were of a basic toxicity equal to or above that of strains which were associated with typical gas gangrene. In their opinion the deciding factor in the production of gas gangrene was the state of the wound. In cases in which *Clostridium welchii* multiplied in the wound without causing gas gangrene, they argued that "the organisms did not find the necessary conditions of anaerobiosis, food supply *et cetera*, to create the massive growth with evolution of toxin which alone seems to enable them to attack living tissue and set up gas gangrene". I think a more likely and simple explanation of these cases was that the strain multiplying in the wound belonged to my proposed third group, and therefore lacked the power to invade even damaged tissue to any great extent, so that a rapidly spreading infection could not occur even if growth in dead tissue did take place.

Further, Robertson and Keppie's contention that massive growth with evolution of toxin must always occur before *Clostridium welchii* can attack living tissue is not supported by the occurrence in man of gas gangrene following hypodermic injections and other trivial injuries.

Practical Applications.

In some hundreds of abortional infections due to *Clostridium welchii*, and in the limited number of post-traumatic cases studied in this laboratory, a close correlation has been observed between certain characteristics of the infecting strain, other than toxin production, and the severity of the resulting infection. This correlation, combined with the observation that washed bacilli from many strains of *Clostridium welchii* were pathogenic for the guinea-pig, calls for a broader outlook in regard to *Clostridium welchii* infections in general. As long as attention is focused only on the toxin production of the infecting strain and on the nature of the wound, our understanding of *Clostridium welchii* infections will be incomplete. It cannot be stressed too often that the invasiveness of the infecting strain is of great importance in regard to both the development and the severity of a *Clostridium welchii* infection.

Any method, therefore, which enables one to determine the invasiveness of the individual strains, will be of practical value in the management of *Clostridium welchii* infections in the human subject.

While the probable virulence of any particular strain can be determined by studying the behaviour of cultures of the organism, such methods are usually too slow to be of much assistance in diagnosis. For this purpose the examination of stained smears from the supposedly infected tissue is to be preferred. The examination of direct smears will show, not only the presence of *Clostridium welchii*, but also the amount of capsular material and the state of the leucocytes. These observations give a fairly reliable measure of the invasiveness of the *Clostridium welchii* present, and they are of diagnostic significance provided one allows for the different susceptibilities of the various parts of the body.

Severe *Clostridium welchii* infections associated with childbirth or abortion occur only when the strain present is of extremely high virulence, since the uterus is relatively resistant to *Clostridium welchii* infection. In such cases the examination of cervical smears provides a rapid means of determining the probable invasiveness of the infecting strain. In severe infections the smears show heavily capsulated *Clostridium welchii* together with damage to the leucocytes (Butler[12]).

The peritoneal cavity is even more resistant to *Clostridium welchii* infection than the uterus. In our experience at this hospital, the presence in the peritoneal cavity of even the most highly pathogenic *Clostridium welchii* rarely results in peritonitis. Certainly the presence of any but heavily capsulated *Clostridium welchii* is of little or no significance. The resistance of the peritoneal cavity to *Clostridium welchii* infection is apparently not always recognized, although it has been well demonstrated by Meleney *et alii*[8] and by Altemier[9] in their studies of peritonitis following appendicitis.

On the other hand, voluntary muscle which has been damaged by trauma or by interference with the blood supply *et cetera* is noticeably susceptible to *Clostridium welchii* infection. In wounds of the extremities, where considerable tissue damage has occurred, strains of only moderate virulence may cause gas gangrene. In such wounds the presence of heavily or moderately capsulated *Clostridium welchii*, irrespective of the condition of the leucocytes, indicates the probability of gas gangrene, and if phagocytosis is poor or absent and if there is considerable damage to the leucocytes, a rapidly spreading infection may be regarded as almost a certainty. The presence in a wound of uncapsulated *Clostridium welchii* organisms which are being actively phagocytosed, suggests at most a mild local infection.

In trivial wounds, in the absence of interference with the blood supply, the detection of heavily capsulated *Clostridium welchii* indicates the possibility of a serious infection, while the presence of large numbers of such *Clostridium welchii* organisms, together with damage to the leucocytes, strongly suggests an active infection, probably of a fulminating character. The presence of poorly capsulated organisms is of little significance.

In an annotation in *The Lancet*[10] as recently as March, 1943, it was stated that hitherto the surgeon had received comparatively little help from the bacteriologist in the early diagnosis of gas gangrene. If attention is given to the amount of capsular material and to the interaction between the bacilli and the leucocytes, as revealed by the examination of direct smears from wounds, such statements will no longer be justifiable in connexion with *Clostridium welchii* infections.

Although the examination of direct smears is essential for early diagnosis, the isolation and study of the strain present should not be neglected, especially in cases in which the examination of smears fails to give a clear-cut result. In cases in which very few *Clostridium welchii* organisms are seen in the smear, or in which, in the presence of heavily capsulated *Clostridium welchii*, phagocytosis or the state of the leucocytes is uncertain, further smears should be examined in a few hours.

In the assessment of the value of prophylactic measures, determination of the invasiveness of individual strains is important. Credit for the success of prophylaxis in individual cases should depend on the isolation from the tissues of *Clostridium welchii* of sufficient virulence to have caused an active infection in that particular situation. In such cases not only smear examinations, but a complete study of the isolated strain should be made.

To determine the value of any particular form of treatment in active *Clostridium welchii* infections, knowledge of the invasiveness of individual strains is essential. It is difficult to determine the efficacy of treatment in a large series of cases unless the proportion of infections caused by highly invasive strains is known, since infections caused by such strains are likely to be more resistant to treatment than those in which the infecting organism only causes a spreading infection when it is able to gain a foothold in devitalized tissue. Kelly's[11] observation that infections following hypodermic injections failed to respond to X-ray therapy, whereas in his experience the majority of post-traumatic infections responded satisfactorily, may have been due to the fact that, in the first type of case, infection was caused by highly invasive strains, whereas in the majority of the cases of post-traumatic gas gangrene the infection was caused by strains of only moderate virulence.

No method of treatment employed at the present time appears to be really effective against the highly invasive variants of

Clostridium welchii, to judge by the extremely high mortality rate in the severe puerperal and abortional infections and in gas gangrene following minor injuries and hypodermic injections.

In the recording of the results of experimental *Clostridium welchii* infections designed to test therapeutic substances, the strains used should be fully described. The need for knowledge of morphology, cultural characteristics *et cetera* has been stressed in a previous publication.[2] The work recorded in the present paper suggests that it is also necessary to use freshly isolated strains in such experiments. That this is not generally recognized is apparent from the many recent articles dealing with the treatment of experimental gas gangrene with the sulphonamide drugs. In these articles it is unusual to find any statement that the strains used were recently isolated from cases of gas gangrene in man; in many instances the experiments were carried out with stock laboratory strains. In Sandusky and Meleney's review[13] of the recent literature on experimental gas gangrene, an attempt was made to explain the different results of various workers; but no mention was made of the possible importance of the period elapsing between the isolation of the strain and its use in experimental infections.

Summary.

1. Washed bacilli from 49 out of 73 freshly isolated strains of *Clostridium welchii* were pathogenic for guinea-pigs.

2. Twenty-five of the pathogenic strains were retested at intervals of three months. After eighteen months only three of these strains still killed guinea-pigs when washed bacilli were used.

3. The ability of washed bacilli to produce a fatal infection in the guinea-pig was more common than were those characteristics indicating a high degree of invasiveness for man.

4. The mode of development of *Clostridium welchii* infections in man is discussed. It is suggested that *Clostridium welchii* strains are divisible into three groups on the basis of the invasiveness of the bacilli themselves: firstly, those strains which can invade healthy tissue; secondly, those which can invade only damaged tissue; and lastly, those which cannot invade even damaged areas.

5. Methods for determining the invasiveness of individual strains of *Clostridium welchii* are indicated, and attention is drawn to the importance of these methods, both in rapid diagnosis and for the assessment of treatment.

6. The necessity for using freshly isolated strains in experimental infections is stressed.

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THE CONCENTRATION AND DRYING OF SERUM FOR INTRAVENOUS USE.

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A METHOD of preparing sterile dried human serum by precipitation of the serum proteins with organic solvents after preliminary concentration of the wet serum in "Cellophane" casings is described in this paper. Hardy and Gardiner,[1] in 1910, in a study of the various protein fractions in plasma, dried small volumes of plasma free from esters by precipitation in the cold with a mixture of alcohol and ether. Further experimental work was later carried out by Hartley,[2] who used various solvents including acetone and ether for the precipitation. Hall, Fader and Decherd[3] have lately used this method for the drying of human serum; but they found difficulty in drying larger volumes of serum (500 to 700 cubic centimetres) owing to the denaturation of the protein which occurred during precipitation as a result of the warming of the solvent.

As the volume of organic solvent needed for precipitation of the protein is ten times that of the original volume of serum, a simple and quick method of concentrating serum is desirable. The concentration of fluids in "Cellophane" bags suspended in a rapid current of air, as described by Kober[4] in 1917, has lately been used by Thalhimer[5] and Aylward Mainwaring and Wilkinson[6] for the aseptic concentration of both human serum and plasma. It has been found to be a simple and inexpensive method, which requires little or no personal attention and can be used to prepare concentrated serum for intravenous use or as a preliminary step in any drying process.

Methods.

Concentration of Serum.

The serum was concentrated in seamless synthetic casings imported from the United States of America, as it was impossible to obtain seamless "Cellophane" tubing manufactured locally or to find a satisfactory method of making "Cellophane" tubing with a water-resistant seam from sheet "Cellophane". The casings used were 23·5 inches long and 3·5 inches wide and each contained when assembled 900 cubic centimetres of serum. Prior to use the tubes were washed inside and out with pyrogen-free distilled water. One end was then sealed by a double fold held in place with a metal clamp. The other end was tied to a glass chimney approximately four inches long and two inches wide and closed with a cotton wool plug. The casing was then wrapped in gauze and paper and autoclaved at fifteen pounds' pressure for twenty minutes. The serum was siphoned aseptically into the casing, the cotton wool plug reassembled and covered with a sheet of "Cellophane" and the casing hung in a rack, which was placed about eighteen inches from the front of an electric fan. A radiator was placed between the fan and the casings, so that the temperature of the air surrounding the casing was maintained at approximately 25° C.

Under these conditions water is lost from the serum at the rate of 13 to 16 cubic centimetres per hour in the first twenty-four hours, so that 600 cubic centimetres of serum can be concentrated under these conditions to half its original volume in eighteen to twenty-four hours. If the concentration is continued to one-third or one-quarter of the original volume, the rate becomes slower. The serum must be placed in the casings before they dry after the autoclaving, as the skins, if allowed to dry after being wet, become very brittle and liable to crack.

Drying of Serum by Hardyization.

Sterile dried serum was prepared by modifying the method originally described by Hardy and Gardiner and using the apparatus shown in Figure I. The solvent was cooled and the protein precipitated by the addition of concentrated serum to ten volumes of a mixture consisting of seven volumes of absolute alcohol and three volumes of ether. The precipitate was then filtered on a Buchner funnel, washed with ten volumes of cold dry ether and dried. The apparatus consisted of two sterile jars of four litres capacity into which the alcohol mixture and the ether were filtered through a Seitz E.K. filter pad.

[1] This work was carried out under a grant from the National Health and Medical Research Council.

These jars were immersed overnight in a freezing mixture of ice and salt; the mixture was replenished in the morning and allowed to stand for two or three hours.

The temperature of the solvent must be −12° to −14° C. before the serum is added, and the whole process is carried out in a refrigerator at 0° C. The jars are connected to the bottle containing the concentrated serum and to the eight-inch porcelain Buchner funnel. The funnel is seated in a wooden ring and the top is provided with a rubber washer surmounted with a copper plate. Both are kept in place by bolts fitted with wing-nuts. Two inlets are provided in the cap through the rubber stoppers X and Y. The inlet Y is used as an air inlet. A number 1 Whatman filter paper is placed in the dry funnel and the covers are placed in position. The apparatus is autoclaved in sections and then connected as shown (Figure I).

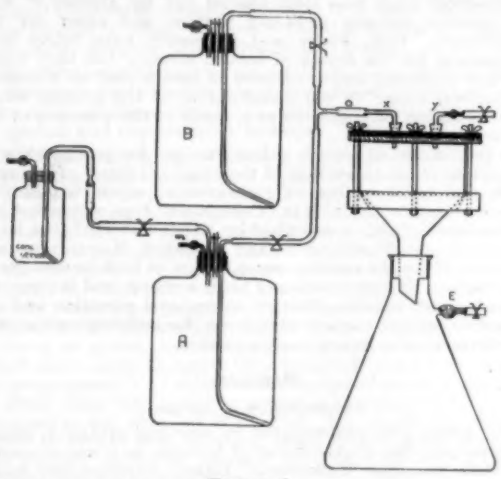

FIGURE I.

The serum previously concentrated to one-third of its original volume and cooled to 10° C. is added to the alcohol-ether mixture at the rate of 10 cubic centimetres per minute. During the addition of the serum to the mixture the jar must be well shaken. After the mixture has stood for two hours the precipitate and supernatant fluid are drawn into the funnel by negative pressure at "E" or positive pressure is applied by means of a hand pump at "M". After jar A is emptied three litres of ether are drawn into the funnel from jar B to wash the precipitate. When filtration is completed a screw clip is placed at "O", and the apparatus is disconnected at this point. The funnel is removed from the flask, its end plugged with sterile cotton wool and the ether is removed from the precipitate by placing the funnel in an evacuated desiccator for twenty-four hours. On removal from the desiccator the dried serum is removed with a sterile spoon into a "Soluvac" bottle. The dried serum is then stored in these bottles till required for use. It is then reconstituted and administered from the same bottle.

Results.

The sterile dried serum obtained by this method is a very fine "off white" powder having a large surface area. After the addition of distilled water or isotonic saline solution, the powder dissolves instantly on shaking, yielding a perfectly clear reconstituted serum. The dried serum has been reconstituted in five minutes to one-half or one-third of the original volume of the wet serum.

The results of one of a series of analyses carried out on serum and on the same serum dried and reconstituted to its original volume are shown in Table I. These analyses show that the protein content of the serum remains unchanged. There are a pronounced diminution in the urea, non-protein nitrogen, potassium, sodium and chloride content of the serum, and a complete disappearance of the alcohol-soluble constituents, cholesterol and lipide phosphorus. No difference has been observed between the agglutinin titre of the wet serum and that of the same serum dried and reconstituted to its original volume, while if the serum is reconstituted to half its original volume the titre is doubled. These results shown in Table II have been obtained with group A, B and O serum.

TABLE I.

Analysis of Wet Serum and of the same Serum after Concentration, Drying and Reconstitution in Distilled Water to Original Volume.

Constituent.	Original Serum.[1]	Reconstituted Serum.[1]
Total protein	6·6	6·3
Albumin	4·9	4·7
Globulin	1·7	1·6
Non-protein nitrogen	29	9
Urea	44	13
Calcium	11·3	9·8
Potassium	27·6	13·1
Sodium	294	100
Chloride	367	106
Inorganic phosphate (acid-soluble)[2]	6·8	6·2
Lipide phosphorus[2]	5·7	Nil
Cholesterol	200	Nil

[1] Results of protein estimations are given in grammes *per centum*; all other results are in milligrammes *per centum*.
[2] As milligrammes of phosphorus.

It was found that the group-specific titre-reducing effect of serum of group A and B, which has been observed by Bryce and Jakobowicz,[7] was unchanged by drying of the serum by hardyization. Group O serum (0·1 cubic centimetre) with an anti-A titre of one-sixty-fourth and an anti-B titre of one-sixty-fourth, was put up with 0·1 cubic centimetre of wet group B serum (titre one-sixty-fourth). Similarly, 0·1 cubic centimetre of the same group O serum was put up with 0·1 cubic centimetre of the same group B serum dried and reconstituted to its original volume. The mixtures were allowed to stand at room temperature for two hours and then titrated with group A and B cells. The results are shown in Table III, and the observed reduction in the titre of the group O serum is the same whether it is mixed with wet or dried group A or B serum.

Reconstituted hardyized serum has been given to 51 patients who, apart from two patients suffering from nephritis to whom serum dried and reconstituted to half its original volume was given, can be classified as suffering from shock. While it is not possible to assess the part played by different factors, such as blood loss, protein loss and trauma *et cetera*, in producing the symptoms of shock, the one constant finding has been the lowered blood pressure; this factor has been used in this series of cases as the chief indication for the administration of serum. This series includes four patients with severe burns, fourteen with post-operative shock, fourteen with traumatic shock associated with fractures, nine with general peritonitis, and three patients who had had a hæmatemesis. Four of these patients were given

TABLE II.

Agglutinin Titre of Wet Serum and same Serum Dried and Reconstituted.

Group.	Anti-A Serum.			Anti-B Serum.		
	Wet Serum.	Serum Dried and Reconstituted to Original Volume.	Dried and Reconstituted to Half Original Volume.	Wet Serum.	Serum Dried and Reconstituted to Original Volume.	Dried and Reconstituted to Half Original Volume.
Group A				64	64	128
Group B	A₁ cells: 32 A₂ cells: 16	32 16				
Group O	1,024	1,024	2,048	32	32	64

TABLE III.

Reducing Effect of Dried and Wet Serum of Group O.

Titre.		Mixed with Serum.				Titre after Standing Two Hours at Room Temperature.		Calculated Titre.	
		Wet.		Dried and Reconstituted to Original Volume.					
Anti-A.[1]	Anti-B.[1]	Anti-A.	Anti-B.	Anti-A.	Anti-B.	Anti-A.	Anti-B.	Anti-A.	Anti-B.
64	64	32		32		32	8	40	32
64	64					32	8	40	32
64	64	1,024	32			516	32	536	48
64	64			1,024	32	516	32	536	48
64	32		16			4	16	32	20
64	32				16	4	16	32	20

[1] Anti-A = group B serum; Anti-B = group A serum.

serum reconstituted to half its original volume, and one was given serum reconstituted to one-third of its original volume. No unfavourable reactions attributable to the serum were recorded. Seven patients suffering from general peritonitis died, and eight others who were already *in extremis* when the transfusion was started also died. Temporary improvement was shown by some of these patients after the administration of serum, generally 600 cubic centimetres; but death occurred some twelve to twenty-four hours later. It is possible that if larger volumes of serum had been given to these patients the outcome would have been different. The improvement in the patients' condition in the remaining cases was generally spectacular after the administration of serum, and from this limited series the impression is gained that badly shocked patients should be given at least one litre of serum, the first 600 cubic centimetres of which should be given rapidly.

Discussion.

The advantages of this method of drying serum are the appearance of the product, the ease with which the dried serum can be reconstituted and the clearness of the reconstituted fluid. This clearness is due partly to the absence of fat and other lipoid material, but also to the absence of denaturation of the protein. It should be mentioned that if the solvent is not properly cooled and the serum is not added slowly, a product which is hard to dissolve and gives a turbid reconstituted fluid may be obtained. The disadvantages of this method are the cost of the large volumes of ether used and the difficulty of aseptically transferring the dried product from the funnel to the bottle in which it is stored and reconstituted before administration. Since January, 1941, 90 pints of serum have been dried by this method, of which 80 have been reconstituted and given to patients. The reconstituted serum was invariably found to be sterile when tested as a routine measure by incubating 20 cubic centimetre samples for twenty-four hours and then subculturing them in anaerobic meat and glucose broth. Economy of solvent is effected by the preliminary concentration of the serum to one-third of its original volume in "Cellophane" casings, and there appears to be no great difficulty in recovering the ether if the process is carried out on a large scale. The cost of each "Cellophane" casing was fourpence, and so far no attempt has been made to use the casings more than once. The other main cost in concentration is the heating of the draught.

Summary.

1. A method of drying serum by precipitation of the serum proteins with alcohol and ether after preliminary concentration in "Cellophane" casings is described.

2. This process, which is known as hardyization, gives a finely divided product which can be dissolved readily, giving a perfectly clear reconstituted serum.

3. The method so far has been used for drying 600 cubic centimetre lots of serum.

4. No difference was observed between the serum protein concentration, the serum titre or group-specific reducing power of the wet serum and that of dried serum reconstituted to its original volume.

5. The advantages and disadvantages of the method are discussed.

6. The results of the administration of 80 pints of the reconstituted serum to 51 patients suffering from shock are discussed.

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Reports of Cases.

ACCIDENTAL VACCINAL INFECTION OF SPECIAL INTEREST FROM THE IMMUNOLOGICAL ASPECT.

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THE following two cases illustrate (i) the ease with which the diagnosis of accidental vaccinal infections may be made by the use as a culture medium of the chorio-allantoic membrane of the chick embryo and (ii) the fact that accidental infection may occur even though the person concerned may be presumed to be highly immune.

Case I.

Mr. F., aged fifty years, had been successfully vaccinated during the war of 1914-1918. His duties in the animal house of the Commonwealth Serum Laboratories included the care of rabbits on which vaccinia virus was being tested for potency. On September 15, 1942, he complained of a painful thumb, stating that he had first noticed the pain two or three days earlier, and that he thought he had pricked the thumb on a thistle. The condition was diagnosed as a septic infection, but it did not respond to foments.

On September 16 the lesion consisted of a small white bleb with a little surrounding redness and swelling. From this bleb a small amount of clear fluid was withdrawn. Part of this fluid was used in two rabbits for Paul's test, part was used for inoculation of nutrient broth and of serum-agar, and a third part was used to inoculate the chorio-allantoic membranes of three developing chick embryos twelve days old. Approximately 0·05 millilitre of a 1:20 dilution in saline solution was the inoculum on each membrane.

TABLE I.

Showing the Production of Hirst's Phenomenon by Virus Isolated from the Cases Recorded.[1]

Origin of Virus Grown on Egg.	Serum Added.	Dilution of Suspension of Virus.									
		1:2	1:4	1:8	1:16	1:32	1:64	1:128	1:256	1:512	1:1024	Control.
Calf lymph ..	Nil	+++	+++	+++	+++	+++	+++	+++	++	+	0	0
Calf lymph ..	Specific anti-serum (calf) 1 : 10	+++	+++	±	0	0	0	0	0	0	0	0
Mr. F	Nil	+++	+++	+++	+++	+++	+++	+++	+	0	0	0
Mr. F	Specific anti-serum (calf) 1 : 10	+++	+++	+	0	0	0	0	0	0	0	0
Mr. F.	Normal serum (calf) 1 : 10 ..	+++	+++	+++	+++	+++	+++	++	+	0	0	0
Mrs. T. ..	Nil	+++	+++	+++	+++	+++	+++	+++	++	+	0	0
Mrs. T.	Specific anti-serum (calf) 1 : 10	+++	+++	0	0	0	0	0	0	0	0	0
Mrs. T. ..	Normal serum (calf) 1 : 10 ..	+++	+++	+++	+++	+++	+++	+++	++	+	0	0

[1] The technique of the test was similar to that described by Nagler.[2] After the serial virus dilutions (0·25 millilitre) were made, an equal volume of saline solution or serum was added to each tube and the whole was incubated at 37° C. for thirty minutes. Then 0·25 millilitre of a 2% suspension of chicken red cells was added and the results were read after further incubation at 37° C. for one hour. The tubes were shaken after serum or saline solution had been added and after the red blood cells had been added. The notations used in the third to thirteenth columns indicate the strength of the agglutination.

The Paul's test yielded a negative result. In the nutrient broth and on the serum-agar no growth occurred. The eggs were examined forty-eight hours after inoculation, and scattered to semi-confluent foci indistinguishable from those characteristic of vaccinal growth were seen on the membranes. These foci, when suspended either in saline solution or in glycerol and applied to the shaven skin of a rabbit, gave rise to lesions characteristic of vaccinia. A typical Hirst's phenomenon[1] was produced by a suspension of the virus obtained from the fourth egg passage and was specifically inhibited by anti-vaccinal serum. In control tests, virus produced by the growth of calf lymph on the chorio-allantois behaved similarly (see Table I).

Case II.

Mrs. T., aged twenty-five years, employed in the ampoule department, had been successfully vaccinated in 1937. When revaccinated by one of us (J.A.B.) in May, 1942, she had yielded a typical complete immunity reaction. On September 24, 1942, she was employed in sealing vaccine lymph in capillary tubes. Twenty-four hours later soreness developed in the thumb and subsequently in the axilla. She reported the condition on September 30; on that date examination revealed a small white bleb with a little surrounding redness and infiltration on the palmar aspect of the distal phalanx of the thumb.

A small amount of fluid (less than 0·1 millilitre) was aspirated from the bleb and mixed with 0·5 millilitre of physiological saline solution. Part of the material thus diluted was used for Paul's test; this test yielded a positive result. Part was used for the inoculation of the chorio-allantoic membrane of the chick embryo. The resultant lesions were similar to those produced by the material in Case I, except that the primary growth was almost confluent. Hirst's phenomenon was produced by the use of the virus obtained from the second egg passage, as is shown in Table I.

On the following day (October 1) more fluid was removed from the original lesion on the thumb and was inoculated on serum-agar. A copious growth of staphylococci ensued. Several of the colonies containing different shades of pigment were all found to be "coagulase-negative", indicating that they were probably not pathogenic.

Comment.

In Case I (Mr. F.), although the Paul's test yielded a negative result, the use of the chick embryo enabled the virus to be cultured without difficulty and the diagnosis to be made with certainty. It must be very seldom that such special culture medium as the chick embryo has been available to clinch the diagnosis of accidental vaccinal infection. No bacteria were grown from that portion of the specimen of fluid which was shown to have contained virus. However, a specimen collected on the following day contained some staphylococci.

In Case II (Mrs. T.) the original specimen was very small indeed. Unfortunately no attempt was made to culture cocci from it. From fluid collected the following day, however, many colonies of non-pathogenic staphylococci were grown.

Perhaps the most arresting feature of these cases is the fact that, in view of her previous vaccinal history, Mrs. T. acquired a vaccinal infection at all. Mr. F. had not been vaccinated since the last war; but Mrs. T. was regarded as being highly immune. She had no recollection of injuring her thumb while sealing the vaccine lymph capillaries, yet a soreness developed within twenty-four hours, and this progressed to a lesion from which virus could be cultivated six days afterwards.

The following case further illustrates the fact that vaccinia virus may survive and multiply in the skin of an apparently highly immune subject, and tends to support the suggestion made by Topley and Wilson[3] of the possible existence in virus diseases of a type of local immunity that is absent in bacterial infections.

Mr. F.M.W., aged twenty-four years, was vaccinated by one of us (J.A.B.) in March, 1942, prior to his taking up duties in the Jennerian department. He showed a typical primary reaction. Since then he has been partly engaged in the preparation and handling of calf lymph, and has been vaccinated on several occasions as a demonstration for medical students (always on the upper part of the left arm at the usual site of vaccination), and each time he exhibited a typical complete immunity reaction.

On April 30, 1943, he was vaccinated on the dorsal surface of the left wrist, and six days later there was apparent a pustule with a surrounding area of redness and induration at the site of vaccination, and the axillary glands were enlarged. A small amount of fluid (about 0·02 millilitre) aspirated from the pustule and suitably diluted with saline solution was used for making laboratory tests. No growth was obtained on blood agar or in nutrient broth, whilst a Paul's test yielded a positive result. Semi-confluent to confluent pocks characteristic of vaccinia resulted from the inoculation of the chorio-allantois with some of the fluid, and a suspension of these ground-up membranes agglutinated fowl red blood cells as strongly as did a culture of vaccinia virus that had been passaged on the egg for several generations.

It is surprisingly easy to keep free from contaminating bacteria virus propagated on the chorio-allantois, and there is little doubt that the membrane deals successfully with a limited number of organisms such as staphylococci.

In order to ascertain the effect on the chorio-allantois of exudate from an ordinary staphylococcal infection, material was taken from such an infection on the hand of a person who had had no known contact with vaccinia virus. This material was subjected to the same tests as were the fluids drawn from the vaccinia patients. Only "coagulase-positive" staphylococci were isolated. At the end of forty-eight hours five out of six embryos, after chorio-allantoic inoculation, were still alive, whilst the membranes were congested, wrinkled and œdematous and contained an abundance of staphylococci. The proportion of embryos that survived for forty-eight hours was quite unexpected.

Acknowledgements.

We are greatly indebted to Dr. C. W. Adey, who made a provisional diagnosis of vaccinial infection in Cases I and II and brought them to our notice.

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DENGUE FEVER.

"It is a singular circumstance that dengue fever is not medically well known. This is not the fault of the individual practitioner, but is principally due to the facts that relatively few have to deal with the disease and that literature on dengue fever is largely buried in journals inaccessible outside large libraries." These words are written by George F. Lumley, Medical Officer of the School of Public Health and Tropical Medicine, University of Sydney, in the introduction to the first part of a "service publication" of that school, issued by the Commonwealth Department of Health under the authority of the Minister for Health. This monograph, for a monograph and a very creditable one it is, has been planned and published to dispel ignorance. Dr. J. H. L. Cumpston, Director-General of Health of the Commonwealth Department of Health, writes in a foreword that of all the factors in the prevention and control of this disease, perhaps the most important is the cooperation of the public, and he adds that the volume has been prepared and presented so that there can be no excuse for ignorance concerning methods of spread of the disease. So that there may no longer be reason for Dr. Lumley's statement, we publish in this issue a special abstract of the monograph. At the same time many will no doubt recall an article on dengue fever by A. S. Walker, E. Meyers, A. R. Woodhill and R. N. McCulloch published in this journal on September 12, 1942. The first part of the monograph, by Dr. Lumley, has been mentioned; it deals with the medical side of the subject. The second part, by Mr. Frank H. Taylor, Entomologist of the School of Public Health and Tropical Medicine, deals with the entomological side. Medical practitioners who have access to the publication will be well advised to read it with care. Dr. Lumley protests that as a compilation the volume is not entirely complete. This may be true, but we agree with him that it is sufficiently complete to constitute "a satisfactory reference". It is a little difficult to see how the contents of this volume are to be brought to the notice of the general public; the work is too technical for the average citizen, and even if it were not, its production in large numbers would be costly and would need a good deal of paper. There are several aspects with which the public should be made familiar; the clinical picture of the infection, the methods of spread and the need for prophylaxis come at once to mind. Dr. Lumley and Mr. Taylor have produced material which writers skilled in the preparation of radio talks and newspaper articles could easily use to advantage.

There is urgent need for the serious consideration of the dengue fever problem. Dr. Lumley states that endemic dengue fever normally excites but little interest. Only when it extends into and even descends as a plague upon non-endemic areas does it produce alarm and are appropriate preventive health measures taken. Readers will remember how the newspapers appeared to vie with one another during the 1942 epidemic to describe the illness, to report its ravages and to give directions for the destruction of the mosquito responsible. Recent talk of malaria has reawakened interest for a while in the mosquito menace, but one has not to look far to realize that the country stands in need of some method that will sustain the public interest in such a matter. Dr. Cumpston in the foreword writes:

> With the high level of general knowledge and education in Australia, and with our efficient system of government, there is no reason why a disease such as dengue fever, with its very definite and restricted method of spread, should be permitted to occur or allowed to continue.

During war, as Dr. Lumley remarks, dengue fever which has often been a scourge in peace time, can cause much greater concern. This is specially true when total war is waged in the tropics and in subtropical districts. "Dengue fever can be crippling to a nation's war effort in the field and on the home front. . . ." The effects of preventive measures are illustrated by reference to papers by J. S. Simmons and his collaborators. They showed that in 1928 the hospital admission rate on account of dengue fever among white enlisted personnel of the American Army in Panama was 0·5‰; among the enlisted white personnel in the Philippine Islands the rate was 177·06‰. Dengue fever occurs in both areas. Simmons and his co-workers believed that in the Panama Canal zone and surrounding areas mosquito prophylaxis had not only resulted in the disappearance of yellow fever and in a considerable decrease in malaria, but had without doubt also been responsible for the extremely low dengue fever rates among soldiers stationed there. They also pointed out that while active mosquito-control work in certain parts of the Philippines had caused a reduction in dengue fever rates, soldiers in Manila could not be protected by control work on army posts alone, if they were continually exposed to great numbers of dengue-infected mosquitoes from other parts of the city.

Reference is made by Dr. Lumley to the epidemic of dengue fever that occurred in 1925-1926 in Queensland and New South Wales. He quotes F. McCallum and J. P. Dwyer, who wrote in this journal that the populations of the districts affected were approximately 425,000 in Queensland and 375,000 in New South Wales. With an attack rate of 70% in these communities a total of 560,000 persons were attacked. During this epidemic there were no large movements of population. It is therefore clear that with the large movements of troops that may and do occur in wartime, an even greater epidemic might occur if conditions prevailed which were similar to those of 1925-1926.

There are several reservoirs of infection. Dr. Lumley mentions four—man, the mosquito (*Aëdes ægypti*, also known as *Stegomyia fasciata*), animals and a possible geographical locality. Man may act as a reservoir in two ways. His blood is infective to vector mosquitoes "upwards of one day during the late prodromal stage and about the first three to five days of the actual stage of illness". Man may also provide a reservoir as a herd in that a sufficient number of recognizable or unrecognizable cases may be suitably spaced to facilitate the virus being carried over from one year to the next. The mosquito, however, is the most important of all reservoirs of the virus. Once infected, it remains infected for the rest of its life. Dr. Lumley points out that it is a fact that an infective mosquito may become non-infective, or an infected mosquito may fail to become infective with the onset of cold weather, in either case developing infectivity when the weather becomes warmer—"two factors largely responsible for the decline and subsequent return of dengue in an area due to the interposition of an unfavourable season of the year". Mr. Taylor describes the endemic areas of Australia and states that he has found *Aëdes ægypti* as far south in New South Wales as Junee and Narrandera.

The School of Public Health and Tropical Medicine has done a service to Australia in publishing this account of dengue fever and its prevention. The disease has, by special regulation under the *National Security Act*, been made a notifiable disease. This is all to the good, but more should be done. Dr. Lumley tells us that measures are being undertaken. In this matter military authorities and public health authorities should act together; and the public must not be allowed to become lax in its war on mosquitoes. Mosquito control should be just as necessary in the eyes of the public as any public health measure, such as the disposal of sewage.

Current Comment.

CANCER OF THE STOMACH.

THERE are few conditions in which physician, surgeon and general practitioner can claim to have a greater interest in common than in cancer of the stomach. All three are faced with the peculiarly difficult problems of diagnosis, and though the surgeon, once the diagnosis has been made, is charged with the removal of the neoplasm, his work is not complete if he disclaims any interest in after-treatment and leaves it entirely to the physician or general practitioner. To be expert in diagnosis a clinician obviously needs more than a knowledge of symptomatology. Physician, surgeon and general practitioner may well take notice of a symposium on gastric cancer published in the June, 1943, issue of *Archives of Surgery*.

Anderson Nettleship writes from the National Cancer Institute of the National Institute of Health of the United States Public Health Service on the subject of experimental gastric carcinoma. He points out that the relative importance of the association of gastric cancer with chronic gastritis, ulcer and environmental factors must be determined. It is sometimes asked what further gain may be expected from animal experimentation; and the reply is that investigators expect to acquire new physiological knowledge and thus to shed light on the pathological processes; in addition, well-defined conditions make it possible to understand and control the agents and to supply unknown links with the idea of instituting preventive measures. One of the most important matters that the investigator has to remember is the time factor. It is not proved that length of time is necessary if extrinsic factors are to act; possibly aging is the essential element. If time rather than aging is of the most importance, experiments which run a year or so might be of use. But in man it would appear that aging is of primary importance. Nettleship thinks that probably the most common error has been the performance of experiments of relatively short duration. In all clinical reports of gastric cancer repeated stress is laid on the length of time during which the "preconditions" exist—the train of events is sometimes thought to extend over twenty years or more. Moreover the average age-specific mortality rate is progressive with age. It has also to be remembered that the complex nature of gastric cancer points to the multiplicity of factors that may contribute to its development. Nettleship states that there are two conditions of the gastric mucosa from which the evolution of cancer is believed to be constant—polypus and *carcinoma in situ* or preinvasive carcinoma; there is also a group of conditions which may result in malignant changes or which are most commonly associated with gastric cancer. The precancerous lesions which may become malignant include chronic gastritis with or without achlorhydria and with or without pernicious anæmia, and chronic ulcer. After describing the environmental and intrinsic factors which affect the mucosa, Nettleship discusses "experimental approaches". He states that it must be experimentally proved whether chronic gastritis is actually a precursor, a cause or simply an associated state. He holds that the question of this relationship still remains an open one. This is borne out by a report by Robert Hebbel published in *The American Journal of Pathology* of January, 1943. Hebbel studied the manifestations of chronic gastritis in 260 stomachs obtained at autopsy, in 106 stomachs resected for duodenal or gastric ulcer and in 52 stomachs resected for carcinoma. Evidence was found to substantiate the view that an antral gastritis and duodenitis precedes and is the anatomical basis for the development of chronic ulcer. In some of the carcinoma-bearing stomachs a diffuse atrophic gastritis antedated the tumours; sometimes the body mucosa was normal or nearly normal; and in other instances the appearances suggested that the mucosal changes were secondary to the tumour, though the possibility of a coincidental association of the lesions was not overlooked. The general conclusion was that there was no evidence to indicate that carcinomata arise with unusual frequency in stomachs which are already the seat of a diffuse atrophic gastritis. But to return to Nettleship. He states rightly that if the association between chronic gastritis and malignant disease can be proved, it will be necessary to discover why the neoplasm arises at a particular spot in a generally damaged mucosa. In this regard secondary factors must be considered—among his "unknown" factors are diet, age, heredity, heat, alcohol, bacteria, virus infection, allergy, and infections of various kinds. At this point Nettleship makes a plea for experimental investigations and here we must leave him.

A. P. Stout contributes a paper to the symposium and discusses the pathology of gastric carcinoma. He deals with those phases which he regards as important in diagnosis and treatment, and bases his article on 225 resected gastric carcinomata and 185 autopsies, 42 of which were on the bodies of patients whose stomachs had previously been resected. Like the other authors mentioned, he emphasizes the statement that it is entirely unknown and unproved whether there is a sequential relationship between chronic gastritis and gastric carcinoma. He points out that the great majority of gastric carcinomata are derived from the mucus-secreting cells of the mucosa. The pyloric end of the stomach is most often affected, and more tumours are found on the superior half of the organ than on the inferior; no part, however, is exempt. He emphasizes the variations in directional growth in different carcinomata and warns clinicians that they must look for cancers in stomachs with gastritis, peptic ulcer and adenomatous polypi. In regard to the histopathology of gastric cancer Stout has found that attempts to predict the degree of malignancy, the rate of growth and the probable success or failure of surgical treatment, based on cellular differentiation alone,

are of little value in an individual case. The microscope can, he believes, best be employed in the study of gastric neoplasms first of all for determining whether or not a lesion is a carcinoma. If the lesion is a carcinoma the direction and extent of spread and the relation of the tumour cells to blood and lymphatic vessels and lymph glands furnish far more valuable information than attempts to determine the percentage of differentiated and undifferentiated cells. Further, he thinks it is not only a waste of time, but also deceptive to attach histologically descriptive adjectives and prefixes to gastric carcinomata. It is far more valuable to describe the gross forms of cancer, since the recognition of these forms is useful in diagnosis and prognosis. He describes four gross types: fungating, ulcerated, spreading and miscellaneous.

L. W. Guiss and F. W. Stewart write on chronic atrophic gastritis and cancer of the stomach. They have studied five groups of stomachs. These included: 35 stomachs from premature infants and from stillborn infants and a few who died soon after birth; 73 "normal" stomachs from persons who had no history or indication of gastric disease; 77 "normal" stomachs from persons who died of non-gastric cancers; 73 stomachs affected by carcinomata; a miscellaneous group of stomachs resected for lesions other than carcinoma. They find no support for the view that chronic atrophic gastritis is a precancerous lesion. The slight difference in incidence of gastric atrophy in cancerous and non-cancerous stomachs in their series was, to them, far from convincing. Atrophic gastritis is an exceedingly common condition in advancing age, and statistical evidence is insufficient to show a causal relationship between it and gastric cancer. It would probably be easy to show that gastric cancer was correlated not only with gastric atrophy, but also with atrophy of other organs and even with such anatomically unrelated structures as genitalia, breasts, circulatory apparatus and skin—reducing to an absurdity conclusions based on statistics alone. To assert on morphological grounds that gastric cancer depends on the existence of gastric atrophy would at least require proof that early gastric cancer begins in and can be traced to an area of atrophy to the exclusion of other areas. Even if this were proved the larger question would still remain as to why one person with gastric atrophy suffered from cancer and another with the same type of atrophy did not.

J. C. Abels, I. Ariel, P. E. Rekers, G. T. Pack and C. P. Rhoads have reviewed recent studies on metabolic abnormalities in patients with cancer of the gastro-intestinal tract. They emphasize the importance of studies of this kind, first of all because they may give some clue as to the cause of the disease, and secondly, because they may yield information by which the morbidity and mortality from operative and radiological procedures may be reduced. They deal in turn with disturbances in the distribution of vitamin *A*, the hypoproteinæmia associated with gastro-intestinal cancer, hepatic dysfunction in patients with gastro-intestinal cancer and metabolic disturbances of the post-operative period. Their general conclusion is that patients with gastro-intestinal cancer suffer from general metabolic abnormalities which may endanger their operative and post-operative course. Many of these abnormalities are probably related to hepatic insufficiency which is most likely induced by the very presence of the neoplasm. The removal of the neoplasm is often followed by a disappearance of the metabolic dyscrasia, and chiefly that which has to do with the fabrication of serum protein. Often dysfunctions, of which hypoprothrombinæmia is the most prominent, persist well into the post-operative period. Total and perhaps subtotal gastric resection, though necessary for the surgical treatment of the patient, may institute a new metabolic disturbance—steatorrhœa and consequent loss of weight. The statement of Abels and his co-workers is justified that a proper recognition of these complications is necessary to the best treatment of the patient.

B. R. Kirklin, writing from the Section on Roentgenology of the Mayo Clinic, discusses mistakes and misunderstandings in the X-ray diagnosis of gastric cancer. He states that it is not necessary to enter a defence for the X-ray method of examination nor to offer an apology for its shortcomings. He holds that the general efficiency and reliability of X-ray examination in disclosing and identifying cancer of the stomach cannot be impugned, and no practitioner of medicine would consider any diagnosis or exclusion of cancer to be complete and convincing without the opinion of a radiologist. But the radiologist is not infallible and is willing to point out his mistakes in the hope of promoting a better understanding with the clinician. One kind of error which Kirklin looks on as indefensible is failure to discover any existing cancer, whatever its size, situation or morphological characteristics may be. X-ray examination will reveal any gastric lesion that is capable of producing symptoms or that can be seen macroscopically; failure to discern it should be charged to the examiner and not to the method. While an explanation can be offered for some errors of omission, for example, in the case of a scirrhous cancer which may not distort the lumen noticeably, or in the case of cancer of the cardia which may not be discovered unless the gas bubble is inspected closely, none are really excusable. Errors of this kind are relatively rare, and probably less than 1% of cancers are not discovered when X-ray methods are adopted. Kirklin discusses the commoner mistakes made in the differential diagnosis of cancer from benign lesions, and mentions as a "prolific source of outright errors, inaccuracies and misunderstandings" the radiological estimate as to the probable resectability of gastric cancer. There is no need to discuss these aspects in detail. Resectability depends chiefly, of course, on the extent of the neoplasm, but it also varies with the skill of the surgeon who is to attempt removal. Some surgeons are noted for their audacity in their surgical adventures and others for their caution. The radiologist is more likely to give what is regarded as a correct opinion if he knows the calibre of the surgeon. Kirklin looks on the fact that resectability varies with the identity of the surgeon as the chief handicap to correct radiological opinions on resectability. It may be that this is so. Because a surgeon attempts to remove a neoplasm and does in fact remove malignant tissue the tumour is not on that account resectable. Another point in the matter of differential diagnosis by radiological means is that the clinician will rely on the diagnosis according to his past experience of the diagnoses given by the radiologist with whom he is working. In other words the skill of the radiologist in matters of diagnosis is as important as that of the surgeon in treatment. And both are liable to make mistakes.

The only other paper in the symposium to which we intend to refer is the final contribution on prognosis and end results. It is written by W. Walters, H. K. Gray and J. T. Priestley, of the Mayo Clinic. It shows at once what medicine has been able to achieve in this important field and also what still remains to be done. From 1907 to 1938 inclusive the diagnosis of carcinoma of the stomach was made at the Mayo Clinic in 10,890 cases. The lesions in 4,648 (42·7%) of these cases were regarded as inoperable and the patients received only palliative medical treatment. The remaining 6,242 (57·3%) patients underwent exploratory operation in the hope that resection might be accomplished. Among this group inoperable lesions were found in 2,431 cases (22·3% of the entire series), and in each instance the incision was closed and nothing further was done. In an additional group of 1,039 cases (9·5% of the whole series) the lesion could not be removed, but some palliative procedure appeared worth while and was performed. In 2,772 cases (25·5%) of the original 10,890 in which the diagnosis was established, gastric resection was accomplished. The mortality rate for all types of resection was 16·2%. This means that only 2,322 of the 2,772 who underwent resection had an opportunity for ultimate cure. Of those who survived operation 28·9% lived five years or longer, 20·4% lived ten years or longer, 15·2% lived fifteen years or longer, 10·5% lived twenty years or longer and 6·3% lived twenty-five years or longer. If a patient lived for five or more years after resection of a gastric carcinoma, the chance of survival during the ensuing years was found to be about the same as for any person of comparable age in the general population.

Abstracts from Medical Literature.

RADIOLOGY.

Development of Bone in Relation to the Formation of Neoplasms.

KEENE O. HALDEMAN (*Radiology*, March, 1943) points out that all bones, with the exception of parts of the skull, are formed by mesenchyme, which first becomes differentiated into hyaline cartilage in the shape of the future bone. The gradual transition of this cartilage into bone begins in the centre and at the ends of the long bones and continues until the attainment of maturity. The majority of bone tumours, both benign and malignant, arise at the site of transition from cartilage to bone, and the neoplastic cell bears a resemblance to the precartilaginous connective tissue, to the cartilage cell or to the osteoblast and osteoclast which are concerned in the actual formation of bone. In general, it may be said that bone tumours are not the result of a failure of the process of bone repair to become arrested, but arise as a distortion of the normal process whereby cartilage is transformed into bone. Strands of embryonic connective tissue near joints, having the power to form cartilage or bone, may give rise to benign osteochondromata or to chondromyxosarcomata. In the small bones of the hands or feet, similar strands of tissue may produce central chondromata. After birth, two types of cartilaginous growth occur. The proliferating cartilage cells on the shaft side of the epiphyseal line may undergo calcification and form an osteogenic sarcoma. The other type of cartilaginous transformation takes place on either side of the epiphyseal line and is characterized by the action of giant cells (or osteoclasts) which cause resorption of the calcified cartilage. This process, when it occurs on the shaft side of the epiphyseal line, may give rise to a bone cyst; when it occurs on the epiphyseal side of the line, to a giant-cell tumour.

Ossifying and Chondrifying Primary Osteogenic Neoplasms.

J. VERNON LUCK (*Radiology*, March, 1943) states that in radiographs taken during the growing years, a localized thickening or elevation of the periosteum, particularly over the metaphyses, should be viewed with suspicion and restudied at close intervals. If the area grows in length or in thickness, it should be considered as a primary malignant bone tumour until proved otherwise. It is unusual to see and diagnose osteogenic sarcoma at this early stage, the pain being insufficient in most cases to bring the patient to a medical practitioner. In the early stages it is not necessary, and frequently not possible, to classify the tumour as sclerosing or osteolytic. It is enough to classify it as osteoblastic sarcoma histologically and as osteogenic sarcoma radiologically. The mere taking of antero-posterior and lateral radiographs of the suspected site is not enough. Films should be taken at various angles, with under-exposures to show soft tissues and over-exposures to demonstrate alterations in densely calcified or ossified areas. Nor is it enough to examine merely the site of a suspected lesion; the opposite side of the body should be studied and in many instances radiographs of the entire skeleton must be made. The clinician should advise the radiologist of his clinical findings and point out the exact site of pain, tenderness and swelling. Persisting, unexplained pain in a metaphyseal region should spur the radiologist to intensive and repeated effort to demonstrate the lesion. When the tumour is palpable and easily visualized, it is already advanced.

The Radiological Diagnosis of Craniolacunia.

J. BLAIR HARTLEY AND C. W. F. BURNETT (*British Journal of Radiology*, April, 1943) state that craniolacunia is essentially an anomaly of the developing vault bones of the fœtal skull. It is usually associated with other congenital defects such as *spina bifida*, encephalocele, hydrocephalus or talipes. It occurs in two main forms, the less marked characterized by depressions on the inner surface of the vault bones, which the authors have proposed shall retain the name of craniolacunia, and the more severe form in which actual areas of absence of formation of the bones occur, which the authors have suggested shall be called craniofenestria. Antenatal diagnosis can be made with relative ease. When craniolacunia is present the shadow cast by the vault of the fœtal skull becomes modified. Instead of being bounded by a smooth and regular margin of even density, interrupted only at the sutures, this margin becomes of variable thickness and density and of irregular shape. In some places it may be duplicated, whilst at others it may be completely defective, so that the position of the sutures is lost; sometimes the suggestion of a reticular pattern may be seen in the vault bones. It thus becomes necessary to identify in all antenatal radiographs the smooth continuous margin of the cranial vault; if this cannot be done the possibility of defective ossification and the presence of craniolacunia must be considered. If these features are seen, together with spinal deformity, they are, in the authors' experience, pathognomonic of this developmental defect. Where spinal deformity is observed or suspected in the antenatal films, it is valuable to try to obtain both an antero-posterior and a lateral view of the fœtal spine, for when reasonably good detail is obtainable it will be possible to estimate whether meningocele or myelocele is present. The authors have found that broadening of the lumbar segment of the spine in the antero-posterior view, with wide separation of the pedicles, so that one obtains the impression as of a sacrum prolonged upwards, always indicates the presence of a degree of *spina bifida*. When deficiency of the pedicles and laminæ can be established in the lateral view, or the bodies of the vertebræ can be seen to lie unduly near the uterine wall, it will be possible to foretell the existence of lumbar myelocele. This curious developmental defect in the skull is in itself of little danger. Its importance is that its recognition in an X-ray examination during pregnancy strongly suggests the presence of some other more dangerous developmental abnormality, on whose account modifications in the conduct of labour might be indicated.

Radiographs Taken after Thoracoplasty.

JOSEPH GORDON AND HENRY K. TAYLOR (*Radiology*, 1943) state that the chest wall following thoracoplasty for pulmonary tuberculosis, as seen radiographically, is generally uniform and regular in outline, the contour of the regenerated ribs merging with the contour of the unresected portion of the bony thorax. In a number of instances, however, they have observed that the contour of the regenerated ribs is disrupted by a degree of outward displacement, which they refer to as an area of "localized lateral convexity". The contour pattern of the regenerating bony cage is greatly dependent upon underlying pleuro-pulmonary conditions. Following the "deribbing" of the thoracoplasty operation, the remaining periosteal bed falls in against the pleural coverings and the lung. Where the pleura is thin and the relaxation of the lung great, regeneration of the thoracic walls results in a hemithorax which is considerably reduced in size. Conversely when the pleura is thickened and the lung densely fibrotic, a lesser degree of collapse results and the regenerating chest wall is not as greatly changed. Should the cavity remain open, either with or without an increase in intracavitary pressure, a barrier is created about which the regenerating bone takes form. Positive pressures have been demonstrated in certain types of tuberculous cavities. Such cavities are notoriously resistant to closure by any means of collapse therapy. The usual line of contour of the reforming ribs is disrupted and a lateral convexity results, which becomes manifest when ossification is completed. This localized lateral convexity was observed after thoracoplasty in 80% of 78 cases in which the sputum was found to contain tubercle bacilli. In the remaining 20% of this group, other sources of tubercle bacilli were found.

Calcification of Renal Tumours.

GEORGE AUSTEN, JUNIOR (*American Journal of Roentgenology*, May, 1943), presents a review of 98 verified malignant tumours of the kidney. Of this group, 16 tumours showed calcium deposits by both radiographic and pathological examination. While the survival rate among those cases in which calcification was not present is approximately 30%, for those with calcification it is 15·3%. Experimental and clinical observation has shown that the pathological deposition of lime salts is dependent upon loss of cellular activity, hæmorrhage, necrosis and hyalinization. Since malignant tumours of the kidney are particularly prone to these degenerative changes, they might be expected to show pathological calcification rather frequently. Although the rate of calcification is extremely variable and not proportionate to the degree of hæmorrhage, it is noted that among the patients who had calcified tumours the duration of symptoms from the onset to the time of treatment was definitely less than among those with non-calcified tumours. On the other hand, the amount of calcium deposited

in a given area is entirely independent of the extent of degeneration, and appears to be governed by some factor or factors as yet undetermined. This feature of pathological calcification is well exemplified in the author's series, where as much (or more) calcium was found in tumours with minimal areas of necrosis as in those with larger areas. Moreover, there seemed to be no direct relation between the degree of hæmorrhage or necrosis and the grade of malignancy as judged by the usual gross and microscopic criteria. Many of the non-calcified neoplasms which were considered comparatively benign by microscopic examination showed equally as much hæmorrhage and necrosis as others which were considered extremely malignant. Likewise, the size of the tumour appeared to have no direct bearing upon the extent of degeneration, the amount of calcification, or the degree of cellular activity, although in general the larger neoplasms showed more extensive necrosis than the smaller ones. Although no positive conclusions as to the prognostic importance of this condition can be derived from the study of such a small series, it appears that the prognosis in those cases with calcification is less favourable than in those without calcification.

Ghon's Tubercle.

ROBERT G. BLOCH (*American Journal of Roentgenology*, April, 1943) states that a revaluation of the so-called Ghon's tubercle or primary tuberculous calcification is needed. In the light of our present knowledge, the only justifiable interpretation that can be placed on the finding of a calcified tuberculous lesion by radiological examination is that it represents the innocuous residual of a tuberculous infection, either a primary infection or reinfection at some prior time, either in childhood or adulthood, without its being possible to determine the time at which the infection occurred. Therefore either the term "Ghon's tubercle" should be dissociated entirely from the time element and applied to all small calcifying or calcified tuberculous foci regardless of age, or if it is to be retained as signifying the residuals of a childhood infection, it should be applied only when the calcified residuals are found in the child.

PHYSICAL THERAPY.

Results of Irradiation Treatment of Cancer of the Lip.

B. F. SCHREINER AND C. J. CHRISTY (*Radiology*, September, 1942) give a survey of 636 consecutive cases of cancer of the lip treated in the years 1926 to 1935 inclusive. All the lesions were proved microscopically to be squamous-cell carcinoma. It was found that cancer of the lip occurred about 38 times more frequently in men than in women, and about 29 times more frequently on the lower than on the upper lip. The treatment must be considered under two heads, treatment of the primary lesion and treatment of metastases to the regional lymph nodes. In the treatment of the primary lesion surgery and irradiation with radium or X rays generally give comparable results. The cosmetic results following irradiation, however, are superior to those of surgery. The treatment of gland metastases was primarily by external irradiation, either X-ray therapy or the radium pack, and occasionally by the implantation of radon seeds or radium needles. It is urged that both surgery and irradiation be employed where indicated, in an attempt to improve the end results when metastases are present. In a group of 334 cases in which there were no demonstrable metastases or enlarged lymph glands at the time of the patient's admission to hospital, prophylactic irradiation was given to the glands in only 59 cases, and in seven of these metastases later developed. In eight other cases in which metastases eventually appeared, no prophylactic treatment had been given to lymph gland areas. The absolute cure rate among the group of 334 cases is 69·5%. If those who died from intermittent disease or were lost to observation with the local lesion healed from two to five years are eliminated, the cure rate is 93·9%. Among a second group of 192 patients with palpable movable lymph glands, some of which were suspected of being metastatic, the absolute cure rate is 68·2%. If those who died from intercurrent disease or were lost from observation with the local lesion healed are eliminated, the cure rate is 85%. Among a third group of 110 patients with fixed metastases in the neck, the absolute cure rate is 10·9%.

Million Volt X-Ray Therapy for Intrathoracic Cancer.

W. L. WATSON AND J. URBAN (*American Journal of Roentgenology*, March, 1943) point out that great advances have recently been accomplished in the surgical treatment of neoplasms of the lung and œsophagus, and at the present time the treatment of early primary intrathoracic cancers is generally conceded to be surgical. Nevertheless the majority of patients when admitted to hospital are in an inoperable state, owing to the extent of their disease, to advanced age with general debility or to a serious concomitant medical disease. X-ray therapy offers a logical form of therapy for the necessarily large group of those with inoperable lesions. It is difficult to obtain adequate tumour dosage in intrathoracic cancer by ordinary high-voltage X-ray irradiation because of the physical and physiological factors involved. The use of higher voltage and greater filtration makes it possible to deliver an adequate depth dose with less reaction in the intervening tissues and skin. The million volt X-ray apparatus which has been in use at the Memorial Hospital, New York, since 1939 delivers 52·4 *r* per minute (in air) at 1,000 kilovolts and three milliamperes, with a filter of two millimetres of mercury, two millimetres of tungsten and eight millimetres of copper, and a half-valve layer of 3·8 millimetres of lead. Between August, 1939, and December, 1940, sixty-three patients with malignant intrathoracic disease were treated with the 1,000 kilovolt machine. The group consisted of 33 patients with cancer of the lung, 21 with cancer of the œsophagus, three with cancer of the lower part of the œsophagus and stomach and six with other lesions, including four patients with pulmonary metastases. Twenty-seven with proved carcinoma of the lung were treated. Symptomatic improvement was noted in eleven patients for an average duration of five months since the beginning of X-ray therapy. Patients with pulmonary metastases have had significant resulting palliation with this type of therapy. One patient with pulmonary metastases from an adenocarcinoma of the rectum which was resected in 1932 had been enabled to lead a useful and fairly comfortable life for a period of two years and ten months with the aid of million volt X-ray therapy.

Effects of Radiation on Workers.

RALSTON PATERSON (*British Journal of Radiology*, January, 1943) discusses the effects of radiation on workers in both the commercial and medical fields. Authoritative work in this field has been done by Goodfellow and Nuttall. Deleterious effects have to be considered under two main heads, firstly, early effects of undue exposure to radiation, and secondly, the late results of long-continued exposure. The late results may be three in number. Firstly, the development of warty growths on the hands and fingers of workers receiving local exposure. These later become epitheliomata. Secondly, anæmia of a lethal type resulting from general exposure to γ rays or from ingestion of radium. Thirdly, the development of tumours in the body itself, as in the bones or lungs consequent on the ingestion or aspiration of radioactive substances. As regards early evidence of undue exposure, the hands may show the effects of ill-advised long handling or mishandling of radium or radon. These effects have been described in detail by Nuttall. The early effects on the blood of general exposure to radiation to an undesirable extent are first seen in the white blood-cell count. Goodfellow has shown that the one constant sign is an absolute and progressive leucopenia due to neutropenia, which if unchecked will reach a dangerously low level. A person who is subject to exposure and whose first leucocyte count was over 6,000 per cubic millimetre is showing early signs of over-exposure if he shows (*a*) a white cell count averaging below 5,000 per cubic millimetre through a series of counts or (*b*) a substantial relative lymphocytosis. It should be presumed that a maintained fall to 4,000 white blood cells per cubic millimetre or lower represents definite and undesirable over-exposure requiring that action be taken. Moreover, at the lower white cell levels the liability to certain infections is increased. All workers receiving local exposure to the fingers must have a regular finger inspection by a competent authority. All workers receiving general exposure must have monthly blood counts as a routine. Working conditions and apparatus must conform to quite elaborate specifications. Paterson emphasizes the importance of enforcing in the commercial field the effective rules of protection already found safe in medical work. The war has increased many fold the possibilities of exposure in industry. One such occupation is that of radium luminizers. Another exists in the use of high-voltage X-ray plants for radiography of welds and castings. Other new processes may be developed.

Special Abstract.

DENGUE FEVER.

IN the leading article in the present issue a reference is made to a service publication issued from the School of Public Health and Tropical Medicine, University of Sydney, by the Commonwealth Department of Health, under the authority of the Minister for Health. The publication is a work of 171 pages and is divided into two parts. The first part is medical, and has been written by Dr. G. F. Lumley; it occupies 141 pages. The second part is entomological and has been written by Mr. Frank H. Taylor; it occupies thirty pages.

Historical.

After a short introduction Dr. Lumley writes a section on the history of the disease. His first reference is to a condition known as *coup de barre* which prevailed at Guadeloupe in 1635 and later; this has been identified as dengue fever. The first experimental work in the transmission of dengue fever was carried out by T. L. Bancroft, of Brisbane, in 1905. (A photograph of Bancroft is reproduced as a frontispiece.) He performed experiments on five volunteers. These persons were bitten by the mosquito *Aëdes ægypti* which had previously fed on dengue fever patients, within the first three days of their illness. Two of the experiments succeeded. Bancroft based no claims on these experiments, but it is pointed out that he worked out a good reason for the incrimination of *Aëdes ægypti* as the vector, and had gone at least half-way towards proving experimentally that the mosquito was the vector. In this section Dr. Lumley describes shortly some of the outbreaks of dengue fever in Australia and leaves the story of the research for a later section.

Geographical Distribution.

The distribution of the disease is described. In the present instance it will suffice to point out that it occurs in the Pacific Islands and in the Far Eastern countries immediately north of Australia. In Australia itself it occurs in Western Australia, from Carnarvon to the Northern Territory, from the Northern Territory to Queensland, with occasional periodic extensions to New South Wales in its northern parts. The coastal belt, from Carnarvon in Western Australia, to Port Darwin in the Northern Territory, to about Townsville in Queensland, is to be regarded as an endemic belt. No endemic area occurs in New South Wales.

Clinical Description.

The following definition of dengue fever is reproduced because it is an attempt to provide a full but concise statement of what is known about the disease:

> Dengue is an exanthematous fever, caused by a specific virus composed of probably differing immunological types; of wide tropical and subtropical distribution in numerous endemic foci, but often occurring therein and elsewhere in epidemic, and at intervals of many years in pandemic, form; usually, biologically transmitted by at least two vectors, the mosquitoes *Aëdes ægypti* and *Aëdes albopictus*—probably others, too; unusually, mechanically transmitted by mosquitoes and possibly other arthropod vectors; the immunity conferred by one attack is highly variable; the disease runs a benign course of days only, being characterized by sudden onset, pain (headache, ocular, muscular, etc.), alterations of taste, rashes, and a normal or lowered leucocyte count; the disease grades down from frank to subclinical to probably inapparent infections; it naturally affects mankind of all races and monkeys of some species; the intrinsic incubation period may be expressed by the formula 3-5-8-15 days; often readily diagnosed, it may defy diagnosis.

Two incubation periods are described. The intrinsic incubation period is that which occurs in man; the extrinsic period occurs in the mosquito. The intrinsic incubation period (with which this monograph is alone concerned) is defined as the period of time elapsing between the times of infection and onset. The onset is established when the temperature rises sharply or even explosively from normal or slightly above normal to attain a high elevation which is more or less sustained, such rise appearing with or following characteristic subjective symptoms, in which event they become accentuated. This definition covers all cases except those in which onset is gradual. Dr. Lumley quotes evidence from the literature in justification of the statement that the incubation period may be expressed by the formula 3-5-8-15; 3 and 15 are extreme limits and the range 5-8 includes the great majority of cases. Nearly 50% of cases develop during the sixth day, approximately 80% have their onset on the fifth, sixth or seventh day, and approximately 90% on the fifth, sixth, seventh or eighth day. There is no evidence to suggest that this time varies according to the vector, so that these figures may be taken as applicable to the disease transmitted by either *Aëdes ægypti* or *Aëdes albopictus*.

The prodromal stage, when present, is included in the incubation period. Opinions vary in regard to the occurrence of prodromata. A prodromal stage may be concealed by its occurrence during the night when the patient may be more or less deeply asleep. And further, patients may be hypersensible or hyposensible. The prodromal stage is regarded as occurring oftener than is usually supposed, probably in more than 50% of cases. It lasts commonly from six to twelve hours, but its range may be from one hour to upwards of two days before the onset. Characteristically it is mild and consists of some combination of headache, backache, muscular pains which are often indefinite, sore eyes, weariness, disinclination for work which becomes burdensome, sensations of chilliness, sore throat, anorexia, nausea, bowel disturbances, giddiness, sleepiness, depression, disturbance of sleep by dreams and nightmares, with or without an associated small febrile response.

The onset is usually sudden. This means that it may occur with great rapidity in the absence of prodromal warning. The words "sudden" or "abrupt" have also been applied to onsets which are dramatic or intense exacerbations of prodromata. Three forms of onset may thus be distinguished: (*a*) the sudden onset with prodromata, which is the commonest, (*b*) the sudden onset without prodromata, which is the most dramatic form, (*c*) the gradual onset in which prodromata gradually merge into the established disease, and this is rather uncommon. The symptoms of onset are headache, muscular pains, prostration which may be associated with a feeling of chilliness, or even a well-developed rigor and sweating.

In regard to the temperature chart a variety of terms are used. The following grouping is stated to cover the findings of most observers: Group 1—the continued fever type; this is uncommon. Group 2—the saddle-back type; in this the temperature gradually declines about the second day, but about the fourth or fifth day when it is nearly normal, there occurs a second sharp rise followed in a day or two by the crisis. Group 3—the interrupted fever or two-phase or diphasic type; this differs from the saddle-back type in that the temperature falls completely to normal by the third or fourth day and rises again on the fourth or fifth day. Group 4—the short fever or one-phase or monophasic type; in this group one wave of fever lasts from one to four days. Dr. Lumley includes among these some of the evanescent or abortive forms of dengue fever. Group 5, which is the afebrile or nearly afebrile type, would include some evanescent or abortive forms and especially the "missed" infections of subsequent attacks.

In describing the rashes of dengue fever, Dr. Lumley points out that some observers have referred to dengue fever as one of the exanthematous fevers. He thinks that there is much to be said for this designation, and on this basis divides the rashes occurring in the disease into enanthemata, involving the mucous surfaces, and exanthemata, involving the cutaneous surfaces and comprising primary or initial rashes and secondary or terminal rashes. Enanthemata, if diligently sought, may, especially in the early stages, be found more often than recorded. They consist of either "an erythema as it were of the buccal and pharyngeal mucosa or a stippling of the soft palate". The primary or initial exanthemata are generally erythematous and occur chiefly on the face, neck and chest; even the back and medial aspects of arms and thighs are sometimes involved. They may be hard to differentiate from heat rashes, and occur as early as 24 hours before the onset of fever. On the other hand they may be very fleeting, and thus may be easily overlooked. Secondary or terminal rashes usually appear from the fourth to the sixth day about the time of the secondary rise in temperature.

Discussion on eye conditions in dengue fever is summarized in the following way:

> 1. The ocular symptoms of dengue fever, such as photophobia, retrobulbar pain, conjunctival congestion, hyperæmia of the optic nerve head, and retinal vascular engorgement, constitute important items in the clinical

picture of the disease, and are useful as an aid in differential diagnosis.

2. Persistent retinal hypersensitiveness may prove annoying under certain conditions, but it subsides spontaneously and is without harmful after effects.

3. Post-dengue accommodative weakness occurs with sufficient frequency to make it important. It is distressing to the patient while it is present, though the degree of discomfort varies with the individual. It may escape detection in certain patients.

4. Well-chosen therapeutic measures can do much to alleviate the distress incident to dengue by minimizing the ocular symptoms.

5. Apparently the unknown toxic agent of dengue has a selective action upon unstriped muscle fibres as evidenced by vasomotor disturbances during the acute stage of the disease and by accommodative disorders following it.

In regard to other features of the disease, it should be noticed that slowness of the pulse is commonly present. Relative bradycardia is almost invariably present during severe attacks while the fever lasts, and an absolute bradycardia is often present during convalescence. Glandular involvement is variable and there is a suggestion that this variability is rather to be noticed as occurring between different epidemics; there is not such variability during one epidemic. The digestive system is almost always disorganized at some time and in some degree. Nausea, vomiting, epigastric discomfort and disorder of the bowels are found from time to time. The condition of the tongue varies between wide extremes. In many cases the tongue is rapidly furred and on the third day may be as thickly coated as that of a neglected typhoid fever patient in the third week. On the other hand, the tongue sometimes remains moist, flabby and perhaps teeth-indented, the fur often looking like a moist coat of whitish or yellow paint. The tip and margins may be clean and red and the tongue sometimes is like the tongue of scarlet fever. Bleeding may occur from the gums in severe cases, and slight hæmorrhage from the rectum is sometimes seen. Involvement of the central nervous system has been stated to be a common feature of dengue fever. Clinicians have claimed that "encephalitis" occurs during dengue fever, and post-mortem evidence is accumulating in favour of some kind of central nervous system involvement. In a proportion of dengue fever cases, the occurrence of one of the several forms of encephalitis may be expected merely upon analogy with other virus diseases. It may be that the causative virus has pantropic characteristics, the neurotropic element of which, usually not evident, may be operative in some cases and thus produce encephalitis. Dr. Lumley concludes that a clinical diagnosis of dengue encephalitis should be only conservatively made, and even then substantial doubt as to its correctness must remain. Albuminuria is stated to be rare in dengue fever, and slight when it does occur. There is, at the same time, evidence that it occurs more frequently than supposed. In regard to the respiratory system, there is good reason to assume that in some proportion of cases of dengue fever there is, contrary to widespread belief, minor involvement of the upper respiratory tract. A leucopenia generally occurs at some time during the course of dengue fever. Complications are unimportant and as a rule there are no sequelæ.

The Attack Rate.

The attack rate is very variable; among the circumstances influencing it are the following: (a) Proportions of non-immune, partially immune and absolutely immune persons among the population exposed; and in some circumstances the period of exposure to infection. (b) The density of the vector. (c) The density of the population. (d) Perhaps properties of the virus of a particular epidemic. Some outbreaks are characterized by a more severe clinical course, so that the percentage of patients seeking medical attention becomes greater. (e) Climatic factors.

Diagnosis.

There are no absolute tests for specific diagnosis of dengue fever. Great difficulty may arise when other readily confusable diseases such as sandfly fever and German measles coexist with dengue fever or when first cases in an epidemic are being discovered. Dr. Lumley gives a formidable list of conditions which must be excluded. Important as it is to establish a diagnosis of dengue fever, it is much more important to avoid the calamity of diagnosing as dengue fever such diseases as smallpox or bubonic plague in their early stages. There is also special interest in the possible confusion of dengue fever and anterior poliomyelitis. The following scheme for diagnosis has been constructed on one presented in 1923 by Rice. First the following epidemiological considerations have to be borne in mind: (a) presence or absence of epidemic or endemic dengue fever; (b) presence or absence of dengue vectors; (c) presence or absence of the vectors of sandfly and relapsing fevers; (d) presence or absence of clinically similar diseases, particularly rubella; (e) climate, including altitude and period of the year. Then come clinical and laboratory considerations. The diagnosis is made on five principal observations, as follows: (a) "sudden" onset with fever; (b) alterations of taste; (c) pains such as headache, ocular pains, generalized or localized pain in the back or limbs; (d) the characteristic facies; (e) normal or lowered leucocyte count. All of these five considerations should be confirmed by (a) a rash; (b) benign course terminating within seven days; (c) absence of marked or rapidly increasing albuminuria; (d) absence of any other disease to explain the symptoms.

Treatment.

For most patients complete rest in bed is necessary. Acetylsalicylic acid is the main therapeutic standby. Sometimes hypnotics are indicated. Prophylaxis will be mentioned later on.

Specific Ætiology.

Dr. Lumley reviews shortly the work done to establish the causative agent of dengue fever. He points out that a cause has been sought among some of the protozoa and the whole range of bacteriological forms—protozoa, spirochætes (including leptospiræ), bacteria, rickettsiæ and virus. He adds that it is incontestable that the causative agent is a virus. He also refers to the size of the virus and its cultivation.

Experimental Transmission to Animals.

Numerous attempts have been made to transmit dengue fever to animals, but no success has attended these efforts. Dr. Lumley states that a number of the negative experiments reported have little or no value at all. There is, however, good evidence that certain monkeys are in some way susceptible to the dengue virus. "It does seem that such monkeys are capable of going through an incubation period, a period of demonstrable virus in the blood stream, and a post-infective stage wherein there is some period of absolute or relative immunity." There is some proof that an animal reservoir for dengue fever can exist, though such a reservoir may be peculiar only to certain but not all endemic areas.

The Role of Mosquitoes in the Transmission of Dengue Fever.

Dr. Lumley discusses in two sections the role of mosquitoes in the transmission of dengue fever. In the first which he devotes to what he calls the first period of research, he deals with work that commenced in 1902 when H. Graham reported his investigations and concludes with the work of J. Burton Cleland and others in 1916-1919. In this period proof was forthcoming that *Aëdes ægypti* is an intermediary host. Possible proof was offered that *Aëdes albopictus* is an intermediary host, and this has since been proved. The view was also rejected that *Culex fatigans* was an intermediary host.

In the second period of research positive transmission by *Aëdes ægypti* as an intermediary host was proved. It is known that an individual suffering from dengue fever is capable of transmitting the virus from his blood to *Aëdes ægypti* feeding upon him in (a) the prodromal stage (up to one day prior to onset of the disease), (b) within the first three to five days of the disease, optimally on the first day, infectivity rapidly declining thereafter to zero. Two considerations require further research. The first is whether the blood loses its infectiousness to mosquitoes when fever disappears. If this did occur, one-day fevers, for example, would have a reduced period of infectivity, whilst a patient in a first wave of pyrexia lasting more than three to five days might have a commensurably prolonged infectivity. In the second place, no specific experiments have been made regarding the possibility of a renewal of infectivity during any secondary rise or return of fever which so commonly occurs in dengue fever. However, there is some evidence of this in an analogy with yellow fever.

Regarding the extrinsic incubation period, it can be concluded on an analogy with yellow fever that for dengue

fever the incubation period in *Aëdes ægypti* is one during which the virus increases in quantity. No evidence exists as to any cyclical development of the virus in the mosquito. On analogy with yellow fever, it may also be assumed that much of the virus, taken up in an enormous number of infective doses, is destroyed or lost in the mosquito and that this is followed by an increase due to propagation of the residual and adapted virus. Dr. Lumley points out that the best work on the duration of the extrinsic incubation period of dengue fever puts the minimum time down at eight days. However, most of the experimental work on this subject has been done with mosquitoes bred and maintained in the laboratory.

In regard to the period during which *Aëdes ægypti* is infective to man, it was found in Manila that *Aëdes ægypti* fed on infective dengue virus was subsequently able to transmit dengue infection between the twelfth and seventieth days. In an investigation in Athens mosquitoes were found to be infective for 174 days.

It has been found that at a temperature averaging 16° C. infected mosquitoes do not develop the capacity to transmit an infection whatever may be the duration of incubation. It has also been found that when the temperature is reduced to 16° C. mosquitoes lose their ability to transmit an infection. At 22° C. infected mosquitoes acquire or recover their infectivity. Such experimental findings are of epidemiological importance in regard to the carry-over of virus from the dengue season of one year to the succeeding season of that or the next year.

Aëdes ægypti feeding on an infective dengue fever patient may take up a large number of infective doses of virus. From this it may be deduced that it is possible for the bite of one infective mosquito to produce dengue fever in man, and experimental evidence confirms this.

Experimental evidence suggests that the virus of dengue fever is not carried from infected *Aëdes ægypti* through its eggs to the succeeding generation, and attempts to transmit dengue virus directly to larvæ of *Aëdes ægypti* have been unsuccessful. Some successful experiments have been performed in which dengue virus was transmitted by feeding normal *Aëdes ægypti* on suspensions of infected mosquitoes. It is believed to be possible that under favourable conditions mosquitoes may become infected with dengue virus through the agency of contaminated food or water.

Evidence is set out showing that when a mosquito takes a partial or interrupted meal of dengue infective blood, many human infective doses must be taken up; a proportion of these must inevitably contaminate the proboscis for some time and be available for infecting any susceptible person upon whom the mosquito resumes its interrupted meal. Dr. Lumley holds that though mechanical transmission is not as a rule important epidemiologically, it may become the sole mechanism of transmission in abnormal conditions which, though unlikely to occur in peace time, may readily arise in circumstances of war. Skin surface contamination with virus is not an epidemiological factor in the spread of dengue.

Reference is made to other mosquitoes as possible intermediary hosts of the dengue virus. Of the various mosquitoes incriminated apart from *Aëdes ægypti* and *Aëdes albopictus*, the most probable vector is *Armigeres obturbans*. Some difference of opinion exists in regard to its distribution and its possible occurrence in Queensland. Further research is needed to determine whether this mosquito can act as an intermediate host.

Immunity.

While little is known about immunity to dengue fever, some advances have been made. It does not appear likely that much further advance will occur until such time as a relatively simple and specific laboratory test for the presence of dengue virus and immune bodies has been developed. Dr. Lumley sets out his conclusions upon the characteristics of dengue immunity on their clinical, epidemiological and experimental grounds as follows: (*a*) Immunity may be evanescent—last weeks only; or prolonged—lasting years. (*b*) It may be partial or absolute. (*c*) Evanescent or prolonged immunity may result from one attack only; but one attack tends to confer a short immunity only. (*d*) Repeated attacks tend to increase the durability of this immunity. (*e*) Maintenance of immunity sooner or later depends upon contracting a fresh infection. (*f*) Subsequent attacks tend to be milder in dengue, grading down from clinically recognisable to subclinical to probably inapparent infections. (*g*) The residents of endemic areas exhibit some degree of immunity; formerly unexposed communities exhibit none. (*h*) The immunity conferred by an attack of dengue is highly individual or variable. (*i*) Whilst the foregoing might possibly be explainable on a basic assumption that there is only one immunological type of the virus, an easier and more attractive explanation can be made on the basis of there being multiple immunological types of the virus.

Epidemiology and Endemiology.

The concluding section of the Dr. Lumley's part of this monograph deals with epidemiology and endemiology. In the leading article in this issue short reference is made to the epidemic which occurred in Queensland and New South Wales in 1925-1926. Mention is also made of the four reservoirs of infection described by Dr. Lumley. In regard to the effects of preventive measures, it only remains to state the three final conclusions:

1. Dengue fever can be controlled by effective preventive methods.
2. Dengue control must be practised by the Services within their own encampments *et cetera*, not only for their own protection but also that of adjacent civilian populations.
3. Still more so must dengue control be practised within civilian areas. This duty devolves upon not only authority, but even to a greater degree upon each individual himself.

Entomological Considerations.

In the first section of Part II, dealing with entomology, Mr. F. H. Taylor describes in detail the genus *Aëdes* and the species *ægypti* and *albopictus*. He also points out that adults of both sexes of *Aëdes ægypti* can live for several weeks or months, but that females are much longer lived than males. Both sexes live much longer in a moist atmosphere. The average length of life under natural conditions is stated probably to be not more than six weeks. Some authors state that the normal range of flight of *Aëdes ægypti* does not exceed 200 yards, but other authors have shown that the flight may extend to 1,000 yards or more. In the leading article in this issue it is stated that Mr. Taylor has found *Aëdes ægypti* in New South Wales as far south as Narrandera and Junee. He publishes a map on which are marked the towns where this mosquito has been found. He regards the abundance of *Aëdes ægypti* in the towns of Temora and Gulgong as very striking, showing that this mosquito has been established in these towns for many years. It may be taken as a fact that towns to the east, north and west, and possibly to the south of Junee and Narrandera are infested to greater or less degree with *Aëdes ægypti*.

Bionomics.

The larva generally hatches on the second day after the egg is laid. The eggs may be kept for several months if they are placed in a moist atmosphere for thirty-six to forty-eight hours before they are desiccated. Unless the eggs are held in a moist atmosphere for this period, the embryo will not have developed sufficiently to prevent collapse of the egg when it is subjected to desiccation.

The time taken by the larva to become full-grown is usually from about seven to ten days under optimum conditions of food and temperature. The pupal period is usually two to three days, but under adverse conditions it may be prolonged.

Only one species, *Aëdes vittatus*, breeds in small rock pools. All the remaining species breed in tree-holes, leaf bases, coconut shells, or similar places holding collections of water, except *Aëdes ægypti*, which breeds in clean water in household utensils and house tanks; occasionally it breeds in tree-holes, but only when denied its natural breeding places. *Aëdes ægypti* never breeds in ground water. It has been found in a puddle hole into which a traveller's water-bag had been emptied. But Mr. Taylor knows of no record where the larva of *Aëdes ægypti* has been found in dirty, much less in foul, water.

Mosquitoes do not feed as often in the winter as in summer. *Aëdes ægypti* requires a blood meal to insure the fertility of eggs before each batch of eggs is laid. Herein lies an extremely important factor in determining the relative decrease in number of mosquitoes in winter.

Control.

It is a simple matter to control and eventually to exterminate *Aëdes ægypti*, provided the assistance of the public is attained and the same directions are always given. The best means to adopt, in addition to the work done by a fully trained staff, is to give detailed instructions in simple language to school children. All receptacles holding clean water in and around buildings are places where larvæ may be found. All disused tins and bottles must be gathered up

and destroyed. The practice adopted by local authorities of dumping such material without destroying it beforehand in swamps and such like places is pernicious. House tanks must be made mosquito-proof. This should be done with wire gauze made from brass or bronze, or if this cannot be carried out, oiling must be undertaken. One egg-cup full of kerosene should be applied once a week to each house tank. All household water containers should be completely emptied once a week. Adult mosquitoes should be attacked with a good quality fly spray in their hiding places, where the direct rays of the sun do not penetrate. Unusual breeding places should be sought and treated.

Correspondence.

REPORT OF THE PARLIAMENTARY JOINT COMMITTEE ON SOCIAL SECURITY.

SIR: May I make some comments on the report published in the journal of July 17, 1943?

A striking feature of this report is its neglect of the views of patients. What they thought, determined the fate of the *National Health and Pensions Insurance Act*: what they think will determine the fate of the medical profession. Not only is their outlook ignored, they are given no say in the administration proposed, save for the suggestion of a layman versed in finance (paragraph 150). Women don't even get that amount of consideration: from the report one would hardly know that women existed, perhaps because they are not the financiers of the nation!

A perusal of the report also shows that domiciliary practice is regarded as hardly existing, instead of being, as it is, a very large part of practice: unless one is to assume that all really ill patients must go into hospital, willy-nilly! and before the doctor sees them. What about the obscure case, the obstetric case which may run into twenty-four hours or even many days? If nurses, junior and senior doctors are all to take their hours and days off regardless of the condition of the patient, each patient being dealt with by a sequence of doctors acting on their predecessor's reports, we shall certainly see an increased death rate, and an excellent illustration of what a novelist makes a doctor (discussing this question) say in a novel I read recently: "There's a great deal of advantage in knowing all about a person." Patients know this even if politicians don't: they will never agree to the change.

In paragraph 149 the control of the services is emphasized. Patients will object to this, too: at present it is between the doctor and the patient, no third party enters in: the doctor advises, the patient decides. In an organization the doctor decides; he also must put the organization, not the patient, first; a third party also may intervene between doctor and patient. The whole relationship becomes a dictatorial one.

That the vocational character of medicine is a sealed book to the committee is evident on reading paragraph 120. They say "it is unreasonable that the doctor . . . should be expected to give his services free to any section of the people". That a vocation should maintain the worker is, no doubt, true, but that medical men and women should so depart from the traditions of millenniums as to accept this saying (nothing for nothing) is incredible. Even to surmise that we could do so is to show the vitiation of our outlook by the financial side of government.

There is a true inadequacy of outlook on the committee's part.

Indeed the whole of the report is marred by its financial aspect. In paragraph 72 the committee says clearly that without financial security for all people the irreducible minimum of health cannot be promised. It then ignores the methods of achieving economic security and goes on to deal with medical problems and organization, most of which would settle themselves if the economic and financial factors were properly dealt with, and by the committee's own showing cannot be efficiently dealt with otherwise.

If medical men and women and their patients wish to avoid further regimentation and dictatorship, invading even their sickrooms, they must face up to the primary problem which underlies not only medical but most of our social problems, to say nothing of being responsible for strikes, riots, revolutions and wars.

A committee or royal commission to inquire into our monetary, financial and economic affairs would be more sensible and more effective.

Yours, etc.,

MARY C. DE GARIS.

Geelong,
Victoria,
August 1, 1943.

Naval, Military and Air Force.

APPOINTMENTS.

THE undermentioned appointments, changes *et cetera* have been promulgated in the *Commonwealth of Australia Gazette*, Numbers 196 and 200, of September 2 and 9, 1943.

PERMANENT NAVAL FORCES OF THE COMMONWEALTH (SEA-GOING FORCES).

Extension of Appointment.—The appointment of Surgeon Lieutenant (for Short Service) (Acting Surgeon Lieutenant-Commander) Charles Patrick Cummerford Reilly is extended for a period of two years from 30th October, 1942.

Transfer to Emergency List, etc.—Surgeon Commander (Acting Surgeon Captain) Alexander Scott Mackenzie is transferred to the Emergency List and reappointed for temporary service, dated 26th June, 1943.

ROYAL AUSTRALIAN AIR FORCE.

Citizen Air Force: Medical Branch.

The appointment of Flight Lieutenant C. E. Tilbury (267124) is terminated with effect from 24th July, 1943.

The probationary appointments of the following Flight Lieutenants are confirmed: R. G. Bligh (263611), D. S. Kidd (266325), W. J. Simmonds (276864), J. R. Wadsworth (267086).

The following Flight Lieutenants are transferred from the Reserve with effect from the dates indicated: N. B. Howse (267413), D. F. O'Brien (253180) (19th July, 1943), B. Starr (257522), M. Barry (267236), C. S. Kerr (285947) (2nd August, 1943).

Norman Arthur Albiston, M.B., B.S., D.P.M. (267550) is appointed to a commission on probation with the rank of Flight Lieutenant (temporary Squadron Leader) for part-time duties with effect from 20th July, 1943.

Reserve: Medical Branch.

The following officers are transferred from the Active List with effect from the dates indicated, but will still be employed on part-time duties: Wing Commander A. B. Anderson (291187) (16th August, 1943), Acting Squadron Leader B. T. Mayes (264848) (26th July, 1943).

Acting Squadron Leader B. T. Mayes (264848) retains his acting rank on transfer.—(Ex. Min. No. 255—Approved 1st September, 1943.)

The following are appointed to commissions on probation with the rank of Flight Lieutenant with effect from the dates indicated: John Arnold Struan Robertson, M.B., B.S. (267525), Donald Robert Sheumack, M.B., B.S. (267516), Colin Ray Ratcliff, M.B., B.S. (267517), Hubert Roy Harris, M.B., B.S. (267518), William Leighton Morris, M.B., B.S. (267522), George Frederick Blaxland, M.B., B.S. (268523), John Maxwell Dowling, M.B., B.S. (267524) (27th July, 1943), Stephen Grimwood Barr, M.B., B.S. (267515), Howard Leslie Benn, M.B., B.S. (257556), Rellee George Skinner, M.B., B.S. (267526) (29th July, 1943).—(Ex. Min. No. 257—Approved 1st September, 1943.)

CASUALTIES.

ACCORDING to the casualty list received on September 8, 1943, Captain L. E. Tansey, A.A.M.C., Bellevue Hill, New South Wales, has been reported missing.

Australian Medical Board Proceedings.

TASMANIA.

THE undermentioned has been registered as a duly qualified medical practitioner:

Ostberg, Bernhard Nils, M.B., B.S., 1943 (Univ. Melbourne), Launceston General Hospital.

Obituary.

RALPH ALDERTON BAKER.

WE regret to announce the death of Dr. Ralph Alderton Baker, which occurred on August 9, 1943, at Maryborough, Queensland.

JOHN BARR McLEAN.

WE regret to announce the death of Dr. John Barr McLean, which occurred on September 8, 1943, at Brisbane.

GERALD EUGENE CUSSEN.

WE regret to announce the death of Dr. Gerald Eugene Cussen, which occurred on September 10, 1943, at Melbourne.

Nominations and Elections.

THE undermentioned have applied for election as members of the New South Wales Branch of the British Medical Association:

Whitby, William Thomas, M.B., B.S., 1941 (Univ. Sydney), Finley, New South Wales.

Giblin, Frederick John Dexter, M.B., B.S., 1943 (Univ. Sydney), Saint Vincent's Hospital, Darlinghurst, New South Wales.

Roberts, Alan Peter, M.B., B.S., 1942 (Univ. Sydney), 4, Janet Street, Merewether, New South Wales.

Kater, Norman Murchison, M.B., B.S., 1943 (Univ. Sydney), Saint Vincent's Hospital, Darlinghurst, New South Wales.

McGeoch, Arthur Hector, M.B., B.S., 1943 (Univ. Sydney), Royal Prince Alfred Hospital, Camperdown, New South Wales.

Finlay-Jones, Lionel Robert, M.B., B.S., 1943 (Univ. Sydney), "Hilsyde", Hilder Street, Camden, New South Wales.

Fitzgerald, Gerald, M.B., B.S., 1938 (Univ. Sydney), NX117615 Captain Fitzgerald, 18th Australian Field Regiment, A.I.F., Australia.

The undermentioned has applied for election as a member of the Tasmanian Branch of the British Medical Association:

Davies, Ronald Tregaskis, M.B., B.S., 1943 (Univ. Melbourne), Launceston General Hospital, Launceston.

Medical Appointments.

Dr. Glen Howard Burnell has been appointed Honorary Surgeon at the Royal Adelaide Hospital.

Dr. James Henry Russell Tremayne, in accordance with Section 39 of the *Mental Deficiency Act*, 1920, of Tasmania, has been reappointed a member of the Mental Deficiency Board.

Books Received.

"Pictorial Handbook of Fracture Treatment", by Edward L. Compere, M.D., F.A.C.S., and Sam W. Banks, M.D.; 1943. Chicago: The Year Book Publishers Incorporated; Melbourne: W. Ramsay (Surgical) Proprietary Limited. 8¼" × 5¼", pp. 351, with 171 illustrations. Price: 30s. (A).

"Spectrophotometry in Medicine", being the authorized translation of "*Medizinische Spektrophotometrie*", by Priv.-Doz. Dr. Ludwig Heilmeyer, translated by A. Jordan, M.B., B.S., D.Sc., M.R.C.P. (London), and T. L. Tippell; 1943. London: Adam Hilger Limited. 8¼" × 5¼", pp. 294, with 120 figures. Price: 53s. 6d.

Diary for the Month.

SEPT. 21.—New South Wales Branch, B.M.A.: Ethics Committee.
SEPT. 22.—Victorian Branch, B.M.A.: Council.
SEPT. 23.—New South Wales Branch, B.M.A.: Clinical Meeting.
SEPT. 24.—Queensland Branch, B.M.A.: Council.
SEPT. 28.—New South Wales Branch, B.M.A.: Medical Politics Committee.
SEPT. 30.—New South Wales Branch, B.M.A.: Branch.
OCT. 1.—Queensland Branch, B.M.A.: Branch.
OCT. 5.—New South Wales Branch, B.M.A.: Council Quarterly.
OCT. 6.—Victorian Branch, B.M.A.: Branch.
OCT. 6.—Western Australian Branch, B.M.A.: Council.
OCT. 7.—South Australian Branch, B.M.A.: Council.
OCT. 8.—Queensland Branch, B.M.A.: Council.
OCT. 12.—New South Wales Branch, B.M.A.: Executive and Finance Committee.
OCT. 12.—New South Wales Branch, B.M.A.: Organization and Science Committee.
OCT. 12.—Tasmanian Branch, B.M.A.: Branch.
OCT. 19.—New South Wales Branch, B.M.A.: Ethics Committee.

Medical Appointments: Important Notice.

MEDICAL PRACTITIONERS are requested not to apply for any appointment mentioned below without having first communicated with the Honorary Secretary of the Branch concerned, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

New South Wales Branch (Honorary Secretary, 135, Macquarie Street, Sydney): Australian Natives' Association; Ashfield and District United Friendly Societies' Dispensary; Balmain United Friendly Societies' Dispensary; Leichhardt and Petersham United Friendly Societies' Dispensary; Manchester Unity Medical and Dispensing Institute, Oxford Street, Sydney; North Sydney Friendly Societies' Dispensary Limited; People's Prudential Assurance Company Limited; Phœnix Mutual Provident Society.

Victorian Branch (Honorary Secretary, Medical Society Hall, East Melbourne): Associated Medical Services Limited; all Institutes or Medical Dispensaries; Australian Prudential Association, Proprietary, Limited; Federated Mutual Medical Benefit Society; Mutual National Provident Club; National Provident Association; Hospital or other appointments outside Victoria.

Queensland Branch (Honorary Secretary, B.M.A. House, 225, Wickham Terrace, Brisbane, B.17): Brisbane Associated Friendly Societies' Medical Institute; Bundaberg Medical Institute. Members accepting LODGE appointments and those desiring to accept appointments to any COUNTRY HOSPITAL or position outside Australia are advised, in their own interests, to submit a copy of their Agreement to the Council before signing.

South Australian Branch (Honorary Secretary, 178, North Terrace, Adelaide): All Lodge appointments in South Australia; all Contract Practice appointments in South Australia.

Western Australian Branch (Honorary Secretary, 205, Saint George's Terrace, Perth): Wiluna Hospital; all Contract Practice appointments in Western Australia.

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1. *Kuschinsky G. Arch. F. Exper. Path. Pharm. 1930. 156-290.*
2. *Kuschinsky G. and Oberdisse K. Ibid. 1931. 162-246.*

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